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THE INFLUENCE OF THE SMALL RURAL HOSPITAL ON THE ADVANCEMENT OF SURGERY IN THE NEW ENGLAND STATES*

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AS you have chosen your president from one of the smaller communities, it seems fitting that I confine my remarks to the progress of surgery in this type of community.

I should like to discuss a subject in which I have been greatly interested for a number of years — The Influence of the Rapid and Efficient Development of the Small Community Hospital on the Advancement of Surgery in the New England States.

I refer to the smaller hospitals — those that do not have nurses' training schools and are not large enough to employ interns.

I think I can best illustrate what I wish to tell you in contrasting the limitations of the surgery of twenty-five years ago with that now done in these small rural hospitals, by relating, with your indulgence, some of my own personal experiences during the transitional period from backwoods and kitchen surgery to the high standard of work now to be found in our many small hospitals. I have the greatest faith in these small institutions and the progress they are making.

The following experiences will give a fair picture of what a surgeon who had been trained at the Massachusetts General Hospital had to contend with at the outset of his country practice twenty-five years ago.

One of our first emergency appendectomies in the country was twelve miles from home, on a late winter Sunday afternoon, with over two feet of fresh, soggy snow on the ground. No automobiles could stir. A horse and sleigh was hired at the local livery stable, and twelve miles in three hours was the best the poor nag could do over the hilly road.

The operation was performed on the kitchen table in the superheated kitchen of an old farmhouse. One kerosene lamp held by the father of the patient was the only light. Ether was poured on a bath towel and folded like a tent over the patient's face by the village doctor. The local nurse acted as assistant. The operation went off well, and I made the same time back home in the dark — twelve miles in three hours in two and a half feet of snow.

After this there were several winters of heavy snow, and the Central Maine Power Company's Snowmobile was used for transportation into the country for appendectomies, hysterectomies, cholecystectomies, cesarean sections and other more or less major operations.

Our patients were always safeguarded in their postoperative period by the rule that the local physician must report daily progress by telephone for at least three days. We never had an infection of any kind in these farmhouse operations. Surgical dirt apparently does not exist there.

In summer, when the roads were in good condition, I traveled, in the company of my surgical nurse, with a portable operating table and kit bags supplied with almost everything that a hospital operating room could furnish; these trips were in no way a hardship, but were often stimulating experiences.

Cesarean sections were sometimes a trial. We were called late on one cold November night to perform one on a woman of 52 who had been trying in vain for two days to have her first baby. The house was in a wild and remote section, the nearest neighbor being four miles away. The house consisted of one room and a woodshed.

This huge woman was placed on the kitchen table, which was reinforced by an old door to give it greater width. A lamp was held overhead by the husband, the local physician acted as etherizer and part assistant (he held a retractor under the sterile sheet) and a moronic dwarf was told to squat down under the table to catch the baby when it was delivered. But, at the first trickle of amniotic fluid, which ran down over her, the dwarf screamed, fled from the scene of action and was not seen again for several days. The local physician then took over both the

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lamp and the ether, and the husband received the baby. This woman made a normal recovery without temperature or other complications.

Probably our most strenuous experience, — and the one most charged with human interest, — carried us early in December far north into the real backwoods. Dr. M. of Guilford had operated on his friend, Tom Snow, in the half-loft of a lumber-trading post at North East Carry at the head of Moosehead Lake, 150 miles from our home. Dr. M. was in trouble and needed help.

We took the early morning train for Rockwood, the railroad station across the lake from Kineo. Being fresh from Boston and used to parlor-car travel, I asked the conductor if there was a chair car on the train. He looked at me in some amusement and said: "Young man, if you don't get your shins kicked by the tough lumberjacks aboard, you'll be lucky. They just don't have parlor cars up this way."

A guide with a moose sled met me at the station, and we started to walk across the mile and a half of recently frozen-over lake.

The guide said, "Doctor, this lake has not been frozen over very long. The ice is thin and the snow has blown over some of the thin places. You keep at least thirty-five feet behind me and, if I go down, you beat it back to the shore as fast as you can — and don't look for me."

He led me a winding trail across the lake, with wind and snow blowing so hard that it was difficult for me to see him most of the time. At the Kineo shore I was met by a lad with a pung drawn by two small horses, with hot bricks on the floor for warmth. I was driven past the big Kineo hotel and around under Mt. Kineo, where huge icicles hung in festoons from its thousand-foot walls, and then up the east side of the lake nine miles to the Folsom farm, where I had coffee and doughnuts and climbed into a larger pung drawn by two splendid black logging horses.

The mail usually went from Greenville at the foot of Moosehead Lake to North East Carry over the ice, but this year the lake had not been frozen over long enough to bear the weight of a horse, so we had to drive twenty-eight miles through the woods with no definite trail to follow. It was slow and cold going, and we reached the outpost about 8 p.m., to find a man with a septic wound and a general peritonitis lying on a miserable bed in a half-loft.

While Dr. M. and I were examining the patient, we heard a commotion below. Going down, we found Mrs. Snow putting a plaster cast on a fractured leg and boiling her instruments to tackle a badly lacerated wrist. She said she had not called us because she knew we were busy with Tom and that she was used to doing this kind of surgery, anyway. Incidentally, she had given a four-hour ether to her husband when Dr. M. operated. The man with the lacerated wrist had four severed tendons; Dr. M. and I worked till 1:00 a.m. sewing him up.

After a night with a Levine tube in place, Tom was better the next day, so I left the camp in the late afternoon, leaving Dr. M. in charge.

Bob Gunn, the guide, and I arrived at Kineo House about 9 p.m. We had to rout out the caretaker to light us across the lake in the dark with his powerful acetylene lantern. I slept at Rockwood that night and took the morning train back home.

Forty-eight hours later, Dr. M. called again and insisted that I return to North East Carry, as the patient was worse. The same trip of over 150 miles was again made, over the semi-frozen lake and through the long miles of woods, and two days were spent in the effort to see the patient through without further surgery. Again the keeper at Kineo House was roused out of his warm bed at midnight to guide us across the lake. When I attempted to give him some remuneration for his trouble and hardship, his reply was, "Oh, no, Doctor, I'm doing this for Tom." Such was the spirit of these fine backwoods people; it was in itself a fine reward for my trouble.

Mrs. Snow was a cultured and well educated woman, and yet she courageously led the kind of life she had to lead in that rough place, and also contributed her bit to efficient backwoods surgery.

There have been many other equally interesting episodes, but these few illustrate the kind of experiences that I dare say were common in many parts of Maine, New Hampshire and Vermont in those days, so few years ago.

Today the rural population has become hospital-minded, and, since the roads are now in excellent condition even in winter, major surgery is now done, not in farmhouse kitchens, but in well equipped small rural hospitals.

The woman of 52 who is having her first baby will, we hope, come to a trained obstetrician and have proper prenatal care. And the Tom Snows will not be operated on by a general practitioner in the half-loft of a backwoods trading post but will be flown out to the nearest good hospital for an operation performed by a well trained younger surgeon.

Such are some of the contrasts between the surgery of that period and the present efficient methods of handling the sick.

I should like to picture for you some of the steps in the development of the rural or small community hospital that have made these advances possible.

I can best illustrate by enumerating the difficulties under which these hospitals have grown up and by then showing how these handicaps have been overcome when a well considered plan of procedure is consistently carried out.

By and large, the problems of the small hospital are the same as those in the larger cities, except in degree. The acute nursing shortage and the increase in costs of food and labor are common to all

institutions at this time. The small hospitals, however, have problems peculiar to themselves.

Insufficient financial support limits the procurement of modern equipment. Staffs are often small, — perhaps not more than four or five men, — and many of these are of the older age group who are no longer particularly interested in progressive medicine. Meetings are indifferently attended, if at all, and there is a lack of stimulus to better medicine. Anesthesia services may be greatly limited. Inexperienced assistants are the rule. These facts have in the past noticeably restricted teamwork so that even the most capable surgeon has been handicapped, and the type of major surgery that he could do was therefore limited.

This is the picture of conditions as they have commonly prevailed in the past. Happily, these days of inertia are practically over, and we in the smaller communities can now look with considerable satisfaction on the noticeable, and undoubtedly permanent, advancements in surgical and medical practice in our New England states.

As I am not conversant with conditions prevailing in the more thickly populated states of Massachusetts, Rhode Island and Connecticut, I must base what I have to say on what I know of conditions existing in the more rural states of Maine, New Hampshire and Vermont. For it is in these states that the majority of hospitals of the type I wish to discuss are situated.

This topic, therefore, may well be of only passing interest to those of you who practice in the large cities or in the larger, well equipped hospitals in the moderate-sized towns. But I hope it will be of sufficient interest to those of you who, like myself, practice in the smaller communities in which all the manifest advantages of the large and completely equipped hospital are not always available.

When I say "advantages," I refer not only to physical equipment but also to the very important item of a complete medical consulting service in the fields of urology, dermatology, pediatrics and neurology. Ideal group practice is rarely possible, or at least rarely complete, in the smaller communities; therefore the surgeon must rely more on himself or, in cases of emergency, must obtain his consultation by telephone from the larger clinics.

Before attempting to show you what I believe the small community hospital has done for the improvement of surgery in New England, I think what I have to say may be made more emphatic if I further enumerate some of the difficulties involved in running a small hospital, in order later to demonstrate just what these hospitals have accomplished in spite of their handicaps.

In addition to the limitations of equipment and consulting services already mentioned, we find other drawbacks of equal importance. That these have not been insurmountable is a fine tribute to community spirit, local pride and the earnest efforts of a few farsighted physicians.

The nursing problem has often been desperate. The younger group of recent graduates are inclined to remain in the larger cities where they received their training rather than to return to their home towns, where working hours may be longer and the pay smaller. As a result of this situation, the small hospital has to use the services of an older and perhaps less well trained group of women who are less familiar with modern trends in medicine and surgery and are therefore less able to be of valuable assistance to the hospital staff. However, I am happy to say this is not a handicap that affects too many hospitals, for many of our small institutions are headed by one or more extremely capable nurses of long experience, sound judgment and marked executive ability.

Having now enumerated some of the various handicaps under which the small hospital labors, I would like to show you how they have been overcome to a large extent.

It is a gratifying fact that a marked change has taken place in the development and growth of most of these hospitals. Their improvement has increased surgical efficiency and enhanced their contributions to medical progress so that they are now maintaining a standard of professional service that closely approaches the ideals of the larger medical centers.

The small community hospital, located in towns of from 5000 to 20,000 inhabitants, exerts a definite improving influence on local medical practice in many ways.

It tends to bring about a better selection of physicians and makes available a larger proportion of the better qualified physicians. It stimulates a desire on their part to pool their skills and experiences and in this way promotes the growth of professional excellence to a degree that would never be possible through attempts to practice individually.

Many of the rural hospitals have originally been proprietary in type and have been founded and staffed by older physicians who have been wise enough to appreciate the vital need of adequate hospital facilities for their particular community. These hospitals have started as very small units, but with the realization by interested citizens of their importance to community growth they have increased rapidly from ten-bed to fifty-bed capacity in comparatively short periods of time.

The progress possible in even very small communities is exemplified in a town of 1500 inhabitants located about thirty-five miles from my home. Ten years ago one of our fine old-school physicians of sixty-odd years had a vision and started a six-bed hospital in a large house on the outskirts of the town. A few years later, a progressive young physician arrived and took charge of its surgery. Being not only cautious but eager to learn, he sought

help in his difficult cases, acting as assistant in the major procedures until he had learned how to do them himself.

Today, this little hospital has sixty beds. It is full at all times. It is equipped with x-ray, a laboratory, an electrocardiograph, basal-metabolism apparatus and a small blood bank. It has regular staff meetings and a good medical library, and has kept out of the red — all because of the vision of an old man and the energy of a young one.

It is also a gratifying fact that since the end of the war the smaller hospitals are attracting an increasingly larger number of the younger and better trained men who are desirous of practicing in the smaller communities — provided that they can find hospital conditions adequate for an increasingly better type of medical practice. These younger men, by virtue of their more recent and advanced training, have seen the necessity for adequate x-ray and laboratory facilities, and this has resulted in a definite improvement in the character of both medical and surgical practice in places where only the barest of hospital necessities were formerly provided.

I am intimately acquainted with a dozen or more such cottage hospitals that started with inadequate equipment and staffs and have, under the guidance of one or two able physicians, grown to be most efficient units and have become stimuli to expanding health activities in their communities. I have witnessed their slow and often painful beginnings, with inadequate financing and outdated equipment. I have appreciated these difficulties and have often been amazed at the progress they have made when certain well-thought-out plans of development have been strictly adhered to.

Probably one of the most vital factors in the building of a successful community hospital is the organization and skillful guidance of the staff. This is accomplished only through great patience, much foresight and real leadership by one or two intensely interested physicians. To overcome jealousies, to avoid favoritism and to keep a staff keyed up to a high degree of efficiency is no mean task.

In evaluating the quality of work done in these small hospitals, which have reached a recognized standard of improvement, I attribute their success largely to the following facts and procedures. That 100 per cent perfection is not obtained one must admit, — but the over-all picture is extremely gratifying when one analyzes the progress made in the past twenty-five years.

The contributing factors have been: the possession of adequate x-ray, laboratory, anesthesia and operating-room services; an intelligent and co-operative superintendent; the formation of a friendly, co-operative and scientifically minded staff group; and consistent adherence to the following staff program:

Weekly staff meetings, at which all important cases and mortalities of the past week are fearlessly and frankly discussed in great detail, — in a spirit of helpfulness and not of destructive criticism.

The privilege of, and the constant use of, a plan of staff consultation on any case, charity or private, at any time of the day or night, when such consultation is indicated.

A staff audit. In an increasing number of hospitals with which I am familiar the reputation of the staff meetings as conferences at which cases are discussed with real scientific interest has spread abroad, with the result that every staff meeting has become a teaching clinic to which physicians come regularly from surrounding towns as much as twenty-five miles away.

The procedure, already established in a few hospitals, is rapidly spreading to other units in even smaller towns, and a praiseworthy effort at real progress is already evident.

I should like to discuss in more detail the staff audit, which in the small institutions has been considerably modified from the original conception of an audit as proposed by Dr. Panton several years ago.

Dr. Panton's audit had as one of its purposes the rating of physicians with a view to future staff advancement. The audit as now used in our small hospitals has no such purpose but confines its aims to the improvement of the over-all hospital service and the hospital records. It seeks to uncover mistakes in diagnosis, errors in judgment and results of treatments and thereby to facilitate a more accurate estimate of the kind of work done by the staff as a whole.

The procedure is as follows: An auditing committee meets each week and makes a careful scrutiny of all records for that week. Cases are first arranged under the specialties: medical, surgical, gynecologic, obstetrical, pediatric, orthopedic, E.N.T. and ophthalmologic. Facts are gathered with the purpose of seeking the following information:

Is the case one of emergency — or is it elective?
Are laboratory and x-ray data sufficient?
Have indicated consultations been held or not?
Were there any errors of judgment or treatment?
Is the record well organized and complete?
What is the result at the time of discharge?
In the case of a death: Was it inevitable, preventable or justifiable?

If, after such an analysis of each record, errors of any kind are found, a notation is made on the record and it is handed back to the physician responsible for it. This is entirely confidential between the auditing committee and the physician.

At the end of each month these weekly audits are broken down and the work of the hospital for

that month is graphically presented in such a summary. At the end of the year the monthly audits are similarly treated, thus furnishing an accurate over-all picture of the kind of work done in each hospital.

The benefits are obvious. Greater frankness in case-reporting at staff meetings has resulted. The percentage of staff consultations is increased; this adds up to a modified form of group practice, which has great advantages for the patient, the staff members and the reputation of the hospital for conscientious and high-type work.

These seem to me to be the most vital factors in the building up of a successful small community hospital. I have faith in the ability of these hospitals to continue to furnish an increasingly higher type of medical and surgical service, provided that a definite and well-conceived plan of procedure is consistently carried out.

However, for its complete accomplishment, and for the maintenance of a high degree of efficiency, the plan must have the enthusiastic support of the younger group of more recent graduates who are equipped with the most recent advances in medical knowledge.

With the advantage of the new blood of the younger men added to the stabilizing influence of the older groups, medicine and surgery in the smaller communities of the New England states are rapidly being advanced to a position where they can show progress and results comparable to those obtained in the largest medical centers.

This fact suggests one more consideration, which I will mention briefly. It is true, I believe, that there is a belief among the older surgeons, especially in the larger teaching centers such as Boston, that there should be cultivated in the minds of the younger surgeons and recent residents a desire to get away from the big city and to seek suitable locations in the smaller communities where well trained and keen young men are so much needed.

Opportunities are just as great in the smaller areas as they are in the larger. There is a wealth of material. The opportunity for the highest type of surgery is likewise just as great as in the larger centers.

It is possible to make a good living, free from many of the drawbacks and complications of big-city practice. There is more leisure in which to become acquainted with one's family, and easier access to the out-of-door recreations, which give needed refreshment. There is also the stimulating effect of working with a smaller group of men in a place in which one can feel that he is making a definite contribution to hospital and surgical advancement.

These are some of the outstanding advantages of small-community practice. It has been one of the purposes of my remarks to point this out to you so that your influence may be brought to bear to urge more of the young men to seek these opportunities.

Under such circumstances, there would seem to be no reason that the patient of small means should be obliged to go to the much more expensive city hospital for a major operation when it can, in most cases, be adequately handled near his home.

The rural population dreads contact with the large, impersonal, expensive city hospital; it misses the close contact with its family and its own physician, — factors that are of vital importance in recovery.

These may seem to some of you to be very minor considerations, but they are nevertheless a definite reason that more and more major surgery is — and will be — done in our now well equipped and adequately staffed small hospitals.

I believe that surgery in New England has already been, and will continue to be, placed on an increasingly higher plane of efficiency, largely as a result of the present promising development of the small rural hospital — and that this influence may do much to offset the trend toward socialized medicine.

I think we can now visualize, in the surgery of New England, a close approach to the ideals and objectives so wisely aimed at by the founders of this Society. Progress in the art of surgery in these New England states is marching hand in hand with the vigorous growth of the small rural hospital.

PERFORATED PEPTIC ULCER: A STUDY OF THE INDICATIONS FOR NONSURGICAL TREATMENT IN SELECTED CASES*

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SINCE 1892 to 1895,[1, 2] when the first reports of successful suture of perforated peptic ulcer were published, the mortality rate in the surgical therapy of this condition has steadily decreased, as is shown in Table 1, which is a chronologic list of the mortality rates in a series of representative cases reported since 1894. This improvement in the prognosis for patients with perforated peptic ulcer is the result, in large measure, of better operative technic, better anesthesia, a clearer knowledge of fluid balance and of blood replacement and the use of the antibiotics and chemotherapy. Despite this record of improvement there has always been a group who have been dissatisfied with the dictum that operation is mandatory in all cases of perforated ulcer. This feeling of dissatisfaction has been substantiated by the fact that in many instances the perforation has been found to have been already sealed off at the time of laparotomy and the peritoneal fluid in over one third of the patients operated on has been found to be sterile.[7] Furthermore, the cause of death following surgical intervention has by no means always been peritonitis but rather some cardiovascular or pulmonary complication.

TABLE 1. *Mortality in Perforated Peptic Ulcer Surgically Treated.*

AUTHOR	NO. OF CASES	YEAR	MORTALITY %
Richardson[3]	103	1894–1915	44.2
Ulfelder and Allen[4]	334	1916–1940	26.9
DeBakey[5]	15,340 (collected series)	1940	23.4
McElhinney and Holzer[6]	336	1935–1946	10.7
Estes and Bennett[7]	83	1944	8.7
Graham[8]	130	1946	6.8
Baritell[9]	88	1947	1.1
Present series	70	1944–1949	1.4

To advocate nonoperative treatment for certain cases of perforated peptic ulcer is not new. The first report of the successful management of such a case was that of T. Hall Redwood, who in 1870[10] described two patients with perforation of the stomach, one of whom recovered without operation. This patient was a twenty-five-year-old housewife, with a previous history of indigestion, who had a sudden onset of abdominal pain that "doubled her up" and was associated with an abdomen "most tender to touch." Redwood prescribed opium and warm applications and ordered that nothing be given by mouth. The patient recovered slowly, but the correctness of the diagnosis in this case is obviously subject to the doubt of any such clinical diagnosis of peptic ulcer made before the Roentgen era. In the years following this paper reports were published of isolated cases or small series of cases of perforated peptic ulcer treated without operation.[11-17]

Lund,[18] Moynihan[19] and Schnitzler[20] were among the first to describe cases of perforations of the stomach or duodenum that on operation were found to have been sealed with either omental fat, a portion of adherent viscera, the anterior abdominal wall or "layers of plastic lymph as thick as wash leather."[19] Several of these patients were operated on as long as a week or more after the onset of symptoms. Singer[21-23] in 1930 described the "formes frustes" perforations in patients seen late, at which time the initial pain and tenderness had partially subsided. Although many of his patients showed pneumoperitoneum, several were treated conservatively.

In recent years Visick,[24] Taylor,[25] Birks,[26] Bedford–Turner[27] and Bingham[28] have been supporters of nonsurgical therapy. These authors treated most of their patients conservatively, with the exception of those who were unco-operative, those suspected of having large amounts of gastric contents in the peritoneal cavity and those who had recently eaten a large meal. In addition, these workers emphasize the increased risk of operation in elderly patients, and more especially in those with chronic bronchitis, emphysema and chronic cardiac disease. Ulfelder and Allen[4] in 1942 stated their belief that patients seen twelve hours after the onset of perforation should be examined with particular attention to signs of peritoneal localization and that such patients should be evaluated with consideration of nonoperative treatment. These authors favored this conservative course, particularly in the older age group.

At the West Roxbury Veterans Administration Hospital from January, 1944, through December, 1949, 1616 patients were treated for peptic ulcer. In 81 of these a diagnosis of perforation into the peritoneal cavity was made. Seventy of them were operated on and the perforation closed, whereas 11 patients were treated conservatively for various reasons outlined below. Of the 70 patients operated on one died, — an operative mortality of 1.4 per cent. This was a patient who succumbed to peri-

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tonitis eight days after repair of the perforation and one day after gastroenterostomy for pyloric obstruction. Two of the 11 patients treated conservatively died, — a mortality of 18.1 per cent, or an over-all mortality for both groups of 3.7 per cent.

Of the 11 patients treated conservatively (Table 2), 4 made an uneventful recovery; 4 patients who were seen several days after onset recovered after drainage of peritoneal abscesses; one survived who had a subtotal gastrectomy because of repeated bleeding six days after the perforation; and 2 were admitted in a state of severe shock, could not be brought into satisfactory preoperative condition and died without operation.

TABLE 2. *Results in 11 Patients Conservatively Treated.*

4	Uneventful recovery
4	Peritoneal abscess drained with subsequent recovery
1	Recovery following subsequent urgent subtotal gastrectomy for repeated gastrointestinal bleeding
2	Died soon after entry. No surgical operation
11	Total

The diagnosis of perforation was well established clinically in all these 11 patients who were treated conservatively (Table 3). In 2 cases the diagnoses were verified by post-mortem examination and a third by operation necessitated because of bleeding six days after the perforation; this third patient also showed x-ray evidence of pneumoperitoneum at the time of perforation. All the remaining 8 patients presented the classical clinical picture of a perforated ulcer, and 4 showed pneumoperitoneum by x-ray studies. Seven of these 8 patients had a subsequent roentgenographic examination of their gastrointestinal tracts, which demonstrated either a deformed duodenal cap or the crater of an active ulcer. One patient had no gastrointestinal x-ray examination performed after his recovery, nor did he have subphrenic air at the time of his perforation; he did, however, have a characteristic history and consistent physical findings.

The following are case histories of the nonsurgically managed patients with perforated peptic ulcer.

CASE REPORTS

CASE 1. A thirty-two-year-old man was admitted on June 22, 1946. He had suffered from symptoms of peptic ulcer for eleven years prior to entry. Twenty hours before admission he felt the sudden onset of severe abdominal pain. He was admitted in shock, the blood pressure being 80/60 and the pulse 130. His abdomen showed the rigidity, tenderness and absence of peristaltic sounds characteristic of advanced general peritonitis. Despite the administration of 500 cc. of blood plasma, 4000 cc. of a 5 per cent solution of dextrose in water given intravenously, constant gastric suction and 50,000 units of penicillin every three hours, his condition did not improve to the point where operation could be undertaken, and he died sixteen hours after admission. Post-mortem examination showed a perforated duodenal ulcer and generalized peritonitis.

CASE 2. A forty-year-old man was admitted on May 7, 1947. In the past he had had symptoms characteristic of peptic ulcer and fourteen hours before admission had felt the sudden onset of acute abdominal pain. On examination he presented a rigid abdominal wall, epigastric tenderness and absent peristaltic sounds. An x-ray film showed no air beneath the diaphragm but findings consistent with pneumonia in the left lung. Because of the time that had elapsed since perforation, the localization of tenderness and the absence of air beneath the diaphragm, it was reasoned that he had had a small perforation, which had become sealed. He was treated with gastric suction, parenteral replacement therapy, intravenous sulfadiazine and intramuscular penicillin; he was given nothing by mouth. Within two days there was audible peristalsis, and the patient passed flatus by rectum. The pneumonia subsided, and six days after perforation he was eating soft foods. Subsequent recovery was uneventful, and gastrointestinal x-ray studies made three weeks later showed a deformed duodenal cap, consistent with a duodenal ulcer.

CASE 3. A sixty-two-year-old man was admitted on November 7, 1947. He had had symptoms of peptic ulcer for twenty years. Three days prior to entry he had developed sudden severe abdominal pain. On entry the abdomen was distended and tympanitic and tenderness was present over the entire abdomen but most marked in the epigastrium. Audible peristalsis was present, though diminished, and the presence of air was demonstrated roentgenographically under both sides of the diaphragm. Because of the duration of the perforation and the signs of localization, he was placed on continuous

TABLE 3. *Evidence for Diagnosis in 11 Patients with Perforated Peptic Ulcer Treated Conservatively.*

CASE	PREVIOUS ULCER HISTORY	HISTORY AND PHYSICAL EXAMINATION CONSISTENT WITH PERFORATED PEPTIC ULCER	X-RAY FINDINGS OF PNEUMOPERITONEUM	SUBSEQUENT GASTROINTESTINAL X-RAY STUDIES CONFIRMED DIAGNOSIS	DIAGNOSIS MADE AT OPERATION	DIAGNOSIS MADE AT AUTOPSY
1	+	+	−			+ (duodenal)
2	+	+	+	+ (duodenal)		
3	−	+	+	+ (duodenal)		
4	+	+	−	+ (duodenal)		
5	+	+	+	+ (duodenal)		
6	+	+	−			+ (duodenal)
7	+	+	+	+ (duodenal)		
8*	+	+	+			
9†	+	+	+		+ (gastric)	
10‡	+	+	−	+ (duodenal)		
11	+	+	−	+ (duodenal)		

*Had severe coronary artery disease and died of a myocardial infarction several weeks after perforation.

†Bled severely on sixth day after perforation. An emergency subtotal gastrectomy was performed, revealing a large gastric ulcer with a recently sealed perforation.

‡Had a gastrointestinal x-ray 8 days after admission, showing a large duodenal ulcer; later had gastrointestinal bleeding and a subphrenic abscess.

gastric suction, parenteral replacement therapy and intramuscularly administered penicillin. On the twelfth hospital day a left subhepatic and subphrenic abscess was drained. The culture revealed *E. coli* and anaerobic streptococcus. After the drainage of the abscess he made an uneventful recovery. Gastrointestinal series made shortly afterwards demonstrated the crater of a duodenal ulcer.

Case 4. A twenty-six-year-old man was admitted on January 9, 1948. He had had previous symptoms suggestive but not diagnostic of peptic ulcer. Twenty hours prior to admission sudden severe abdominal pain occurred. On entry the abdomen was board-like in its rigidity and there was air under both sides of the diaphragm. Although his blood pressure was 120/80 on admission, his pulse was 140; despite supportive therapy his blood pressure steadily fell to 80/60. Five hours later the pulse was 160. Because of the long duration of the perforation and the patient's very poor physical condition, treatment was conservative. After the drainage of a subphrenic abscess, which on culture demonstrated beta-hemolytic streptococcus, he recovered. Subsequent recent gastrointestinal x-ray studies showed a deformed duodenal cap consistent with an ulcer. On examination three months later he was found to have gained 27 pounds and was feeling well.

Case 5. A fifty-nine-year-old man was admitted on April 17, 1948. He had suffered from symptoms of "stomach ulcers" for twelve years. Three weeks prior to admission he felt the sudden onset of upper-abdominal pain. Since that time he had had chills and fever and the pain had continued intermittently, localized predominantly to the right upper quadrant. On the fifth hospital day a large duodenal ulcer was revealed by gastrointestinal x-ray studies. On the sixth hospital day massive melena occurred. Despite large doses of streptomycin and penicillin the patient continued to have fever until on the sixteenth hospital day a left subhepatic and subphrenic abscess was drained. Convalescence thereafter was smooth, and he left the hospital fifty-two days after admission.

Case 6. A thirty-two-year-old man was admitted on April 5, 1948. He had previous symptoms characteristic of peptic ulcer. A transthoracic vagotomy had been performed in December, 1946, after which his symptoms were entirely relieved until a sudden severe abdominal pain occurred fourteen hours prior to admission. The abdominal wall was board-like in its rigidity. The blood pressure was unobtainable. Despite the intravenous administration of plasma and large dosages of antibiotics the patient failed progressively; he died ten hours after admission. Post-mortem examination revealed a perforated duodenal ulcer and generalized peritonitis.

Case 7. A thirty-three-year-old man was admitted on April 25, 1948. He had had no previous history of ulcer symptoms. Thirteen hours before admission he noted the sudden onset of severe abdominal pain. On entry tenderness and spasm were localized to the right upper quadrant. Peristaltic sounds were audible. There was air under the diaphragm, as seen in plain abdominal films. Because of audible peristalsis and the localization of the peritonitis, it was presumed that he had had a small perforation that had sealed itself off; he was placed on gastric suction, parenteral nutrition, streptomycin and penicillin. Subsequent convalescence was uneventful, and recent gastrointestinal x-ray studies revealed the duodenal deformity of a chronic ulcer.

Case 8. A thirty-one-year-old man was admitted on July 2, 1948. He had had symptoms of a peptic ulcer for three years. Twenty hours before admission he experienced the sudden onset of severe abdominal pain. Examination on entry showed tenderness localized to the right upper quadrant of the abdomen. Peristaltic sounds were diminished but present, and x-ray films showed a small amount of air under both sides of the diaphragm. In view of these findings it was thought he had had a small perforation that had become sealed off; he was accordingly treated with gastric suction, parenteral therapy and intramuscular administration of penicillin. With the passage of flatus and the return of peristaltic sounds a graduated surgical gastric diet was started. Subsequently the patient went on to an uneventful recovery. Gastrointestinal x-ray studies made shortly afterwards demonstrated the niche of an ulcer in the duodenum.

Case 9. A twenty-six-year-old man was admitted on August 14, 1948. Seventeen hours prior to entry he had a sudden onset of severe abdominal pain. On entry the abdomen showed tenderness localized to the right flank and right lower quadrant. Peristaltic sounds were absent. No air was seen beneath the diaphragm on an x-ray film of the abdomen. It was thought that he had a small perforation that had become sealed off. The patient was placed on a conservative regimen and made an uneventful recovery. The duodenal deformity of an ulcer was demonstrated by subsequent gastrointestinal x-ray studies.

Case 10. A sixty-two-year-old man was admitted on February 10, 1949. Except for one episode of vomiting material with the appearance of coffee grounds he had no previous history of ulcer. The vomiting occurred two weeks prior to his attack of severe abdominal pain, which is described below. He was transferred to the Medical Service from another hospital with the diagnosis of a recent myocardial infarction. This attack was characterized by severe precordial pain and electrocardiographic changes consistent with a myocardial infarction. He had a history of 4 "heart attacks" during the previous two years. Shortly after admission, however, he developed severe abdominal pain and vomiting. Examination showed a board-like abdominal wall, with absent peristaltic sounds. X-ray studies revealed no air beneath the diaphragm. A diagnosis of perforated ulcer was made, and he was treated conservatively with success. He was transferred to the Medical Service, where he had another coronary occlusion two weeks later and died shortly afterwards. No post-mortem examination was obtained.

Case 11. A fifty-eight-year-old man was admitted on March 11, 1949. He gave a history of peptic ulcer of twenty years' duration. He was admitted to the Medical Service with melena and hematemesis, and the diagnosis of a bleeding duodenal ulcer was made. On the fourth hospital day he experienced the onset of shortness of breath and substernal oppression. His pulse was 120, and x-ray films of the chest revealed scattered areas suggestive of multiple pulmonary infarctions. Bilateral superficial-femoral-vein ligation was performed. On March 14, 1949, the patient developed severe abdominal pain. Examination showed a man in shock, with a board-like abdomen and absent peristaltic sounds. X-ray films showed air under both sides of the diaphragm. Because of his critical condition operation was ruled out. A transfusion of 500 cc. of blood was given and gastric suction was instituted. Penicillin and a 5 per cent solution of glucose in water were given parenterally. On this regimen he did well for six days, after which time he began to vomit blood and to have massive tarry stools. A subtotal gastrectomy was performed as an emergency, and a large and effectively sealed off gastric ulcer (1.5 cm.) was revealed, adherent to the liver (Fig. 1). The patient withstood the operation well and made an uneventful convalescence.

Comment

Patients 1 and 6 both arrived at the hospital in shock. Despite all efforts at resuscitation they failed to respond and died without operation sixteen and ten hours respectively after admission. They were not thought suitable candidates for surgical intervention at any time.

Patients 10 and 11 both demonstrate the efficacy of the conservative regimen in the management of the poor risk and the older patient. Although Patient 10 did not live to undergo gastrointestinal series to substantiate the diagnosis, the history and physical findings were consistent with a perforated ulcer. He responded well to the conservative management of his obvious perforation. He died only after another coronary-artery occlusion, several weeks later.

Patient 11 did well for six days on a conservative regimen and at that time underwent subtotal gastrectomy because of recurrent massive hematemesis

and melena.[29] This patient was shown at operation to have a gastric ulcer 1.5 cm. in diameter (Fig. 1), which had become effectively sealed off by adhering to the undersurface of the liver.

Patients 2, 3, 4, 5, 7, 8 and 9 all had perforations of more than twelve hours' duration but with signs of localization; except for the development of 3 abscesses that were later drained, all made uneventful recoveries.

Discussion

From this experience it seems to us that the indications for nonoperative treatment of patients with perforated peptic ulcers are few, but if these indications are heeded the mortality will be favorably influenced. The cases described above, which were conservatively managed, demonstrate that

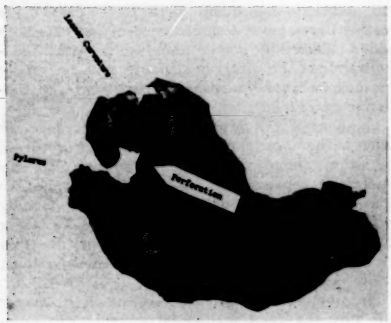

Figure 1. *Photograph of the Subtotally Resected Stomach of Patient 11, Showing the Relative Size of the Perforation, Which Was Sealed Off by the Undersurface of the Liver.*

two other considerations in addition to shock have aided us in the selection of patients for nonoperative treatment. The first is the presence of signs of localization of the peritonitis. This is most frequently seen in patients who have small perforations that have sealed early or in those patients in whom perforations have occurred many hours before treatment is sought. The second is the condition of certain patients, which is so poor that a postoperative mortality is highly probable.

The proper evaluation of the patient who is a poor surgical risk is obviously difficult but is the important keystone of this policy. In our series a recent myocardial infarction was the determining factor in the decision in 2 patients (Cases 10 and 11). Acute pulmonary infection is another consideration that might influence one to contemplate conservative therapy, as it influenced us in Case 2.

The attitude toward conservative treatment that we wish to present is based on a careful evaluation of the individual patient and his individual problem. We are of the opinion that patients with perforated peptic ulcers should usually be operated on and that it is logical to defer operation only in the rare cases in which one is convinced that the perforation has sealed, that the peritonitis has localized or that the patient is too poor a risk for surgical intervention.

Summary

During a six-year period, 81 patients with perforated peptic ulcers were treated at the Veterans Administration Hospital, West Roxbury. There were 3 deaths, a mortality of 3.7 per cent.

Seventy of these 81 patients were treated by surgical closure of the perforation, with one death, an operative mortality of 1.4 per cent.

The 2 deaths in the nonoperative group of 11 cases occurred shortly after admission and were associated with shock due to peritonitis.

On the basis of this experience, it is concluded that nonsurgical therapy for perforated peptic ulcers is advisable in cases in which it is certain that the perforation has sealed, that the peritonitis is localized or that the patient is too poor a risk for surgical intervention.

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CHRONIC DISSECTING ANEURYSM OF THE AORTA RESEMBLING CHRONIC RHEUMATIC HEART DISEASE*

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THE incidence of dissecting aneurysm of the aorta is higher than is usually realized, since it is found at about 1 of 500 autopsies.[1] With increased accuracy in diagnosis more cases of acute dissection of the aorta are being recognized before death. In Baer and Goldburgh's[2] series of 44 cases, 11 were diagnosed ante mortem.

When the characteristic clinical picture of dissecting aneurysm of the aorta occurs, with the development of aortic systolic or aortic diastolic murmurs with a short period of survival, the diagnosis is more obvious than when the patient survives the acute phase and then develops a prolonged course, complicated by cardiac enlargement and congestive heart failure. Acute dissection of the aorta is usually characterized by the sudden onset of excruciating chest pain radiating to the back, occurring most often in a person past the age of 50 who also has hypertension. The electrocardiogram is usually negative, which helps to rule out acute myocardial infarction, although occasionally the dissection may involve the coronary arteries, with resulting electrocardiographic changes.

If the patient survives the initial aortic tear, fever, tachycardia and tachypnea usually develop.[3] If the patient continues to survive, cardiac enlargement and intractable congestive heart failure may develop and dominate the picture. However, this clinical picture and the presence of aortic systolic and diastolic murmurs offer no definite clue to the diagnosis of dissecting aneurysm of the aorta. In fact, such cases simulate other forms of cardiovascular disease. The problem is not a rare one; it is stated that 1 out of 10 patients recovers from acute dissecting aneurysm of the aorta and eventually dies of other causes.[3] Half the patients recovering from one attack of dissecting aneurysm will develop subsequent dissections that cause death. Cases have been recorded of patients with healed dissecting aortic aneurysms, with endothelization of the aneurysmal cavity, who eventually are incapacitated by cardiac enlargement and congestive heart failure.[3, 4]

These cases fall into the group referred to by some authors as chronic dissecting aneurysm of the aorta. Shennan[5] described 66 such cases in his report, 50 per cent of whom died of congestive heart failure after a long period of survival. Gouley and Anderson[6] report 6 cases of chronic dissecting aneurysm of two months' to four years' duration all of whom had cardiac decompensation, which was responsible for their death.

The two cases that form the basis of this paper fall into the classification of chronic dissecting aneurysm of the aorta in which the diagnosis was not obvious ante mortem because of the presence of clinical manifestations resembling rheumatic heart disease. The clue to the diagnosis was further concealed because both our patients were relatively young and had neither hypertension nor the chest pain usually associated with acute dissection of the aorta.

CASE REPORTS

CASE 1. The patient, a 21-year-old woman, was first admitted to the Beth-El Hospital on January 18, 1948, with complaints of fever ranging from 101–104°F. of one year's duration, a backache of five weeks' duration and fleeting migratory joint pains (felt especially in the right shoulder). Prior to this admission she was considered to have rheumatic fever, for which she was treated at two other institutions with no appreciable change in symptoms.

Physical examination revealed a very obese young woman, in no acute pain or distress. The temperature was 100.8°F. Examination of the lungs was negative. Examination of the heart revealed a regular sinus rhythm. No thrills or murmurs were present. The cardiac borders were not accurately percussible because of obesity. The pulse rate was 95 and regular. The blood pressure was 140/85. Examination of the extremities revealed long, tapering fingers with hyperextensibility of the metacarpophalangeal joints. On January 22 a cardiologist noted a blood pressure of 150/90 and a dia-

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stolic blowing murmur audible in the sitting posture over the aortic area and Erb's point, which he considered to be characteristic of aortic insufficiency, probably rheumatic in origin. The temperature was irregular, with alternating flat periods and short periods (1 to 2 days) of low-grade fever. On February 11 the patient complained of a "sticking pain" over the upper precordium, accompanied by dyspnea and restlessness. A neuropsychiatrist suggested that the patient was suffering from an anxiety state and recommended psychotherapy. The patient was discharged on February 21, somewhat improved, with a diagnosis of psychoneurosis, to be followed in the clinic.

She was readmitted in May, 1948, because of a report of a previous skin biopsy that indicated the possibility of a diffuse vascular disease. The fleeting joint pains and the feverish feeling had persisted in the interim following her first discharge. At this time a high-pitched blowing diastolic murmur was heard best at the second left intercostal space and over the aortic area. Some resistance and tenderness was noted over the left lower quadrant of the abdomen. An intravenous urogram revealed a ptosed and rotated left kidney. Examination of the optic fundi was negative. In view of the suggestive skin-biopsy report the patient again was discharged for clinic follow-up. Intermittent low-grade fever persisted, and she was admitted to another institution with a presumptive diagnosis of brucellosis. She again complained of pain in the right upper extremity, and a diagnosis of bilateral cervical rib was made, for which she was operated on. After the operation in May, 1949, the patient continued to feel ill. Four to five weeks prior to her third admission to Beth-El Hospital she was seized with severe tearing pain in the back and chest. The pain lasted approximately one week and required frequent Demerol injections for relief. Accompanying the pain were progressive dyspnea and ankle edema. At the time of her third and final Beth-El Hospital admission on October 2, 1949, the temperature was 103.2°F. and the dyspnea was marked. She complained of generalized abdominal pain and vomiting. A diastolic gallop at the apex and a diastolic blowing sound over the aortic area were noted at this time, with a rapid cardiac rate. The liver was found to be 2 fingerbreadths below the costal margin and was tender. No pitting edema of the extremities was present, although they appeared swollen. The patient was treated for cardiac failure but continued to complain of pain in the chest with dyspnea. Shortly thereafter the patient awoke during the course of a quiet night's sleep with a complaint of severe sudden pain in the chest and died within a few minutes.

A composite résumé of the laboratory data covering the patient's three admissions to this hospital follows: Urinalysis revealed good concentrating power and no significant findings except for an occasional trace of albumin during her first admission. The basal metabolic rate was −3. The erythrocyte sedimentation rate on several occasions during the first hospital admission was within normal limits. With the exception of a moderate leukocytosis on one occasion, hematologic studies were unremarkable. Blood chemistry revealed normal values for glucose, total proteins, albumin-globulin ratio, urea nitrogen and serum chlorides. An Exton-Rose glucose-tolerance test showed normal values. The blood Kline test was negative. An antifibrinolysin titer on February 4, 1948, was ++++. Repeated blood cultures, including anaerobic cultures, were negative. Febrile agglutination tests were entirely negative. X-ray examination of the chest revealed an aortic type of heart of normal dimensions. The lungs were clear except for moderate bilateral hilar thickening and secondary root-branch accentuation. X-ray films of the long bones and a flat plate of the abdomen were negative. X-ray films of the skull revealed moderate thickening of the cortical tables. The sella turcica and sinuses appeared normal. Electrocardiograms made on January 9, 1948, revealed regular sinus rhythm, left axis deviation, a normal PR interval (0.20 sec.) and a prominent S wave in Lead 3; electrocardiograms made on October 2, 1949, revealed a left-ventricular-strain pattern with inverted T waves in Leads 1 and CF_5.

On post-mortem examination the essential positive findings were limited to the cardiovascular system. The parietal pericardium was markedly thickened, roughened and hemorrhagic, and there were numerous fibrinous adhesions to the underlying epicardium (Fig. 1). The heart was enlarged and weighed (with pericardium and entire aorta) 1000 gm. There were no gross signs of chronic rheumatic endocarditis. All valves were normal. The left ventricle was dilated and hypertrophied. There was flattening of the trabeculae carneae. The tips of both papillary muscles on cut section revealed sharply demarcated foci of yellowish-white softening. The myocardium was brown in color and showed no areas of fibrosis. The cusps of the aortic valve were natural, and there was no fusion or separation of the commissures. The left coronary-artery ostium was widely patent and the left coronary artery itself showed minimal sclerotic changes and was widely patent. The right coronary ostium was represented by a small pinpoint opening in the true intima of the aorta that was contiguous with an opening 2 mm. in diameter in the endothelial lining of the aneurysmal sac, which will be described below. The right coronary artery itself was widely patent throughout and showed no sclerotic changes. The right ventricular wall measured 0.7 cm., the left ventricular wall 1.5 cm. There was a saccular aneurysmal dilatation on

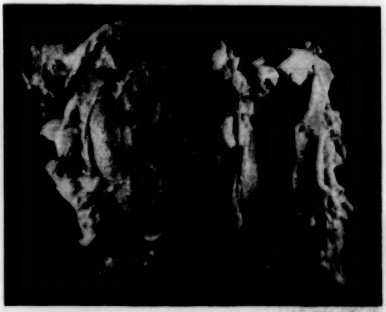

FIGURE 1. *Case 1. Photograph of Heart Revealing the Markedly Thickened, Roughened Pericardium with Fibrinous Adhesions to the Underlying Epicardium.*

A probe is seen in the abdominal portion of the aneurysmal cavity and shows the point of re-entrance of the aneurysm into the right common iliac artery.

the right aspect of the aorta in its ascending portion, which measured 13 cm. across (Fig. 2). There was a dissection of the media of the aorta that extended from the beginning of the aneurysm into the right common iliac artery. This lumen was covered by endothelium and showed fibrous bands extending from the internal aneurysmal lining to the aorta proper. The aneurysmal sac communicated with the lumen of the aorta by a linear transverse stoma 2 cm. in length that was situated 2.5 cm. above the aortic cusps. In the right common iliac artery an irregularly outlined stoma measuring 1 cm. in diameter served as recommunication with the true lumen of the aorta. Both lumina, as well as the aneurysmal sac, contained post-mortem clotted blood. The left inferior margin of the aneurysm projected into the pericardial cavity to the left border of the pulmonary artery. No actual communication can be demonstrated between the aneurysmal sac and the pericardial cavity.

Microscopical examination revealed a subacute pericarditis characterized by infiltration of both parietal and visceral layers of the pericardium by numerous lymphocytes, plasma cells, neutrophils and some macrophages. Abundant recent and old hemorrhage was also present. In the papillary muscle there was a large focus of recent infarction, with extensive coagulative necrosis of the myocardial fibers and infiltration by numerous inflammatory cells, mainly neutrophils. Sections cut through the aortic aneurysm revealed moderate intimal thickening; the lining of the aneurysm was composed of active inflammatory cellular exudate and proliferation of numerous young fibroblasts. Sections from the grossly normal

aortic wall revealed numerous foci of cystic degeneration of the media in which the cystic spaces were filled with basophilic substance (Fig. 3). No reactive inflammatory changes were found in the vicinity of the cysts. The vasa vasorum were microscopically unremarkable. Careful examination of all the other viscera failed to disclose any generalized vascular disease.

The final anatomic diagnosis was: dissecting aneurysm of aorta, re-endothelized, with re-entrance into the right common iliac artery; pericarditis, fibrinosanguineous, secondary to leakage from aneurysm; occlusion of right-coronary-artery ostium; recent infarction of papillary muscles of left ventricle (coronary insufficiency); hypertrophy and dilatation of left ventricle; and bilateral hydrothorax (250 cc.).

CASE 2. The patient, a 38-year-old man, was admitted to the Beth-El Hospital for the first time in March, 1949. He had been in apparently good health until three and a half years prior to this first admission, when he noted the onset of gradually increasing exertional dyspnea and occasional orthopnea, which necessitated giving up his work as a laborer. He was treated at a cardiac clinic of another institution for rheumatic heart disease. For several months previous to this admission he had complained of intermittent pain in

FIGURE 2. *Case 2. Dissecting Aneurysm of Ascending Aorta Showing Small Fibrous Bands Extending from the Aneurysmal Lining to the Aortic Wall.*

the right upper quadrant of the abdomen and of seeing spots and rainbows around lights, with varying degrees of pain in the right eye. For two weeks before admission he had a coryza, cough, pain in the region of the right scapula and substernal pain aggravated by respiration and coughing. There was no previous history of rheumatic fever, hypertension or venereal disease. Review of the patient's family history revealed that his father had died of a stroke. His mother was alive and well, as were his child and wife. Physical examination at the time of the first hospital admission revealed a well developed and nourished man, moderately dyspneic and appearing acutely ill. His temperature was 103.4°F. Examination of the lungs revealed dullness at both bases posteriorly with diminished breath sounds, increased tactile fremitus and vocal resonance. Showers of crepitant rales were present over both bases posteriorly. Examination of the heart revealed enlargement to percussion both to the right and to the left. Regular sinus rhythm was present, with a rate of 96. A loud, harsh aortic systolic and an early aortic diastolic murmur were heard over the entire precordium, best in the second and third right intercostal spaces, and transmitted to the neck. A systolic thrill was palpable at the right sternal border in the second and third intercostal spaces. The blood pressure was 110/58. Examination of the abdomen revealed a sense of resistance in the right upper quadrant. Funduscopic examination revealed marked venous pulsations and moderate arterial pulsations bilaterally.

Blood chemistry and blood count were within normal limits. Sputum examination revealed a culture of pneumococcus but was repeatedly negative for acid-fast organisms. A blood Mazzini test was negative. Repeated electrocardiograms revealed a left-heart-strain pattern. X-ray films of the chest made on several occasions revealed an aortic type of cardiac enlargement with evidence of pulmonary congestion. Repeated blood cultures were negative. The erythrocyte sedimentation rate, venous pressure and repeated urine examinations were within normal limits.

The patient was treated for pneumonia with penicillin and responded in two days, with the temperature becoming normal and with subsidence of the pulmonary findings. The cardiac status responded favorably to digitalis and mercurial diuretic therapy. The patient was considered to have rheumatic heart disease with aortic stenosis and insufficiency. He was readmitted in July, 1949, stating that two weeks after his previous discharge from the hospital he had become

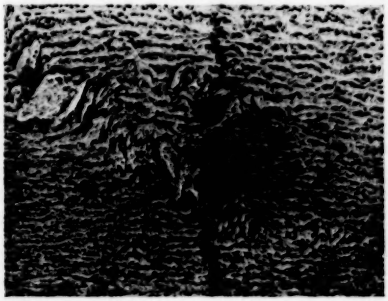

FIGURE 3. *Case 1. Section from a Grossly Normal Portion of the Aortic Wall Revealing Numerous Foci of Cystic Degeneration in the Media in Which the Cystic Spaces Are Filled with Basophilic Material Without Inflammatory Reaction.*

increasingly dyspneic and orthopneic, with frequent attacks of paroxysmal nocturnal dyspnea and palpitation. While he was at home there had also been a short unspecified period of low-grade fever.

Physical examination at this hospital admission showed the patient to be dyspneic, orthopneic and afebrile. The pulmonary signs noted previously had cleared, but there was still dullness at the right base posteriorly, with diminished tactile fremitus and vocal resonance. Occasional crepitant rales were heard at both bases posteriorly. Examination of the heart at this time showed the point of maximal intensity to be in the sixth intercostal space, with the presence of the thrill and murmur as previously noted. Regular sinus rhythm was present, with a rate of 88. The blood pressure was 106/40. Examination of the abdomen revealed a firm, slightly tender liver edge 3 fingerbreadths below the right costal margin. Slight ankle edema was present. Laboratory studies revealed the same x-ray and electrocardiographic findings as previously. The blood count, blood chemistry and erythrocyte sedimentation rate were within normal limits. A spinal-fluid Wassermann test was negative, and the spinal-fluid chemical findings were within normal limits. The patient responded well to bed rest, digitalis and mercurial diuretic therapy and was discharged as improved one week later.

The patient's final admission to the hospital was in September, 1949. He stated that two to three weeks after his previous discharge from the hospital he had again become increasingly dyspneic, orthopneic and weak. He had also had right-upper-quadrant abdominal pain and fullness and had become completely bedridden.

Physical examination at this time revealed him to be more dyspneic and orthopneic than previously. The temperature was normal. The blood pressure was 100/40. The physical

findings and laboratory data, including the electrocardiogram, were practically unchanged from those of the previous hospital admission. The patient was again given digitalis and mercurial diuretics in addition to oxygen, bed rest, sedation, salt-free diet and so forth but failed to respond. The patient died one week after this admission.

On post-mortem examination the pertinent positive findings were limited to the thoracic cavity. The pericardial sac contained a small amount of amber-colored fluid. The heart was markedly enlarged, weighing 740 gm. The cardiac chambers were not unusual, with the exception of the left ventricle, which was markedly dilated. The left-ventricular myocardium was moderately thickened, measuring 2 cm. in average diameter. The posterior papillary muscle of the left ventricle revealed dense fibrotic foci near its tip. The valves showed no pathologic changes. The aortic valve cusps were thin and pliable. There was no fusion or separation at its commissures. The ostium of the right coronary artery, in contrast to the widely patent left-coronary ostium, was markedly narrowed and surrounded by a puckered aortic intima. The most marked changes were present in the aorta. The ascending aorta was the site of a large aneurysm that bulged toward the right of the right-auricular appendage. Two cm. above the aortic valve a transverse tear was found in the aortic wall that entered the aneurysm described in the ascending aorta. On opening the aneurysmal sac it was seen to be lined with a thin glistening membrane and was filled with post-mortem blood clot. Thin strands of fibrous tissue traversed the proximal portion of the aneurysm and ran from one wall of the aneurysm to the other (Fig. 4), 3 cm. below the arch of the aorta. A communication of the aneurysmal sac with the aorta was identified; thus an actual double-barreled aorta is present.

Microscopical findings. Examination of the heart revealed extensive replacement fibrosis of the myocardial fibers at the tip of the papillary muscle. The outstanding changes were found in the aorta. Sections cut through the aneurysmal sac disclosed a relatively avascular collagenous tissue lining the wall of the dissecting aneurysm. In other sections of the aorta numerous foci of vacuolization and cyst formation were found in the media. The cysts were filled with a basophilic, faintly fibrillar material. No sclerotic changes were found in the vasa vasorum in the adventitia. There were no changes suggestive of syphilis.

The final anatomic diagnosis was: dissecting aneurysm, old, of ascending aorta, re-endothelized, with re-entrance into the descending thoracic aorta (double-barreled aorta); stenosis of the right coronary ostium by aneurysm; infarction, old, of the papillary muscle of the left ventricle; and hypertrophy and dilatation of the left ventricle.

Discussion

The clinical picture produced by acute dissecting aneurysm of the aorta has become well recognized, and ante-mortem diagnosis is increasingly more frequent. The group of patients surviving the acute episode has received less attention. The cardiovascular findings may simulate other forms of heart disease. Both patients described in this report were observed over long periods of time by competent cardiologists and in several hospitals. The diagnosis in both cases was rheumatic heart disease. The features of these cases that led to this diagnosis were the age of the patients, the presence of aortic systolic and diastolic murmurs, wide pulse pressure, cardiac enlargement, repeated febrile episodes and congestive heart failure. In Case 1 activity of the rheumatic process was suggested by the fever and migratory joint pains. Other causes of aortic systolic and diastolic murmurs, such as syphilitic heart disease and subacute bacterial endocarditis in particular, could be readily excluded. The possibility of chronic aortic dissecting aneurysm was not suggested in the records of either patient.

It should be emphasized that extensive and repeated aortic dissection can occur without pain. The incidence of painless aortic dissection was approximately 54 per cent in Baer and Goldburgh's[2] series of cases. Both our patients were free of pain attributable to aortic disease during the greater part of their illness. In Case 1 the precordial pain noted five weeks before death was produced by recurrent aortic dissection.

Although dissecting aneurysm of the aorta is commonest after the age of 50, its occurrence in younger patients is not rare. About 24 per cent of the cases have been reported in patients less than 40 years of age,[7] and it has been found at the age

Figure 4. *Case 4. Photograph of the Aneurysmal Sac Revealing the Endothelized, Glistening Lining.*

Thin strands of fibrous tissue are seen traversing the aneurysm and running from one wall of the aneurysm to the other.

of 14 months.[1] The comparative youth of our patients may be noted. Pre-existing hypertension is frequently, but not invariably, present. In Baer and Goldburgh's series, 42 per cent of the cases occurred in the absence of hypertension. Neither of our patients was hypertensive.

Electrocardiographic changes in acute aortic dissection are usually absent. If the dissection does involve the coronary arteries, electrocardiographic evidence of coronary disease may appear. Case 1 revealed no electrocardiographic abnormalities on January 19, 1948. However, on October 2, 1949, the presence of left heart strain and acute coronary insufficiency was demonstrated. These changes were explained by the acute myocardial infarction of the posterior papillary muscle of the left ventricle, which was initiated by the occlusion of the right coronary artery as it coursed through the aneurysm of the ascending aorta. In Case 2 the electrocardiogram showed a left-heart-strain pattern and was also consistent with coronary insufficiency. This finding was compatible with the pathological evidence of dense fibrotic foci at the tip of the posterior papillary muscle of the left ventricle.

Clinical features usually present with chronic dissecting aortic aneurysm include fever, cardiac enlargement, congestive heart failure and aortic systolic and diastolic murmurs. Since these may be the only findings, it may be extremely difficult to differentiate this condition and rheumatic aortic valvular disease. An increased awareness of this diagnostic problem should lead to careful fluoroscopic, roentgenographic and kymographic studies of the ascending thoracic aorta in cases that otherwise would be labeled rheumatic heart disease.

Summary

Two cases of chronic dissecting aneurysm of the aorta are reported in which the clinical features were highly suggestive of rheumatic heart disease.

Both cases occurred in relatively young persons, were not accompanied during the major part of the illness by the typical chest pain of dissecting aneurysm of the aorta and were complicated by congestive heart failure. In neither case was hypertension present.

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TRAUMA OF PHRENIC VESSELS

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THIS report concerns injury to the diaphragmatic vessels by the needle used for thoracentesis. Only three cases have been reported, to our knowledge: one by Elkin,[1] another, which will be described here in detail, and a third suggested by post-mortem findings but not previously reported in the literature. This report is made because of the rarity of the complication and the frequency of thoracenteses.

In a recent issue of the *Journal of the American Medical Association* a case of arteriovenous fistula of the phrenic vessels following thoracentesis was reported. Two years after the chest tap for pleural effusion, a diagnosis of aneurysm of the intercostal vessels was made.[2] However, at operation, twenty-four years after the initial procedure, aneurysm was proved to be present but was found to involve the phrenic vessels.

Case Reports

Case 1. Patient No. 117878, a 27-year-old man, was admitted to the station hospital, Fort Jay, on November 14, 1948, with a two-day history of sharp lower-left-chest pain, nausea and vomiting followed by fever, cough with slight hemoptysis and chills. Physical examination revealed signs of a consolidating left-lung lesion. Admission diagnosis of atypical pneumonia, with pleurisy, was made.

The patient ran a low-grade fever until November 17, when his temperature began to rise and he had increased pain in the lower left chest, after which his temperature fell to normal. On November 21, the patient's temperature suddenly spiked to 104°F., with chills and flatness over the left lower lobe posteriorly. X-ray examination suggested the presence of fluid in the left pleural cavity. A clinical diagnosis of empyema was made, and a diagnostic tap was attempted. A note made by the medical officer at the time of aspiration is quoted as follows:

> Two attempts were made, in each case unsuccessful. No free air was obtained. At end of aspiration approximately ½ cc. of blood was aspirated; however, no free bleeding was encountered. Patient made no complaints and appeared to be in good condition at the time of completion of aspiration. Tap was made in the left 7th interspace just lateral to the angle of the scapula with the patient in the sitting position.

About three and a half hours after the attempted aspiration the patient suddenly felt very faint on going to the bathroom and of his own volition returned to bed. After a second unsuccessful attempt, he began to complain of marked weakness and within the next hour went into severe shock, with a thready pulse averaging 120, a blood pressure at 70/40, pale, cold, clammy skin, dyspnea and marked anxiety. Intravenous administration of glucose in distilled water was started immediately. Fifty gm. of serum albumin was given intravenously. Four and a half hours after the chest tap was made surgical consultation was requested. A diagnosis of intraperitoneal hemorrhage due to the aspiration was made and immediate exploratory laparotomy recommended. The patient was given 1500 cc. of whole blood, the last 500 cc. of which was given under pressure, and the blood pressure rose from 70/40 to 149/90. The quality of the pulse was then improved, although the rate continued to be rapid. The color showed definite improvement; the skin became warmer, and dyspnea and anxiety decreased. Approximately eleven hours after thoracentesis had been performed, operation was begun under local anesthesia.

A left subcostal incision under local anesthesia was made down to the peritoneum. When this was exposed dark blood could be seen within the peritoneal cavity. The incision was then enlarged medially to transect the rectus muscle and laterally along the costal margin. General anesthesia was then induced. The peritoneum was opened, and a large number of liver-like clots were removed from the left infradiaphragmatic space above the stomach, left gutter and pelvis. The liver and stomach were retracted to the right, and active bleeding was found in this area. This was aspirated and sponged dry, at which time a small artery of the diaphragm was found spurting for a distance of about 15 cm. into the left infra-

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diaphragmatic space. Suture of this artery was accomplished with considerable difficulty, as no instrument commonly used as a needle holder was of sufficient length to reach the bleeding left inferior lateral[3, 4] (or posterior)[4] phrenic artery. However, the needle was finally grasped with a ring-sponge forceps and suture ligatures applied. The remainder of the blood was aspirated from the pelvis and several smaller clots were removed from within the peritoneal cavity. Two thousand measured cc. of blood was removed. It was estimated that an additional 500 to 1000 cc. had been lost, but this could not be measured due to the absorption of the sponges and so forth. The ligated vessel was again inspected and found to be dry, after which the abdomen was closed in layers with interrupted sutures of silk, without drainage.

The patient's condition during surgery was good and after surgery a careful toilet of the tracheal and pharyngeal mucous membrane was accomplished. Postoperative recovery was uneventful with regard to the intraperitoneal hemorrhage

On December 23, the lesion that had initially been diagnosed as pneumonia was discovered to have been an early abscess of the lung due to Friedländer's bacillus. After intensive antibiotic therapy, given parenterally and by inhalation, and oral administration of aureomycin, an open thoracotomy was done through the seventh and eighth ribs and the cavity unroofed and packed. After this surgical procedure the patient had an uneventful postoperative recovery except for a transient tension pneumothorax that rapidly responded to underwater drainage.

The abdominal wound healed *per primam*. The thoracotomy cavity closed by granulation, with complete healing of the chest wall. X-ray films show complete clearing of the lung, except for an obliteration of the left costophrenic angle. The patient has returned to full duty and is engaging in his customary activities.

Case 2. The third case referred to was seen by one of the authors (C. F. S.) in France. A 22-year-old enlisted man who had received a penetrating gunshot wound of the left chest at 6 p.m. on September 27, 1944, was received at 7 a.m. on September 28 at the Ninth Evacuation Hospital in impending shock. When the patient's general condition improved a laminectomy was performed to relieve complicating compression of the cord by fracture of the laminas of the second and third thoracic vertebras. The following day the patient seemingly developed a postoperative aspiration-type of atelectasis, possibly due to pulmonary compression by a hemothorax. Although the procedure was made difficult by the condition of the patient, who was lying in the supine position with the injured thoracic vertebras slightly elevated, right lateral thoracenteses just anterior to the midaxillary line were performed, but only a moderate amount of blood was obtained. Posterior thoracentesis was planned for later in the day, but the patient died prior to the time of the contemplated procedure.

In addition to the fractures noted above, as well as extrapleural, subpleural and parenchymal hemorrhage of lungs, atelectasis of all lobes of the lung, slight right hemothorax and small needle-puncture wounds of the liver, post-mortem examination revealed needle-puncture wounds of the right diaphragm corresponding with skin wounds on the right lateral chest wall in the third and seventh intercostal spaces between the anterior and midaxillary lines, with one of the punctures lying just inferior to one of the larger veins of the diaphragm, and hemoperitoneum — 2000 cc. of dark blood and clots. The peritoneum was smooth and shiny; no adhesions were found. There were no wounds in any of the viscera or blood vessels. The comment of the pathologist and prosector was that the hemoperitoneum was an enigma. When this case was reviewed the conclusion was reached that a similar complication of thoracentesis, probably involving a right lateral (or posterior) phrenic vessel, resulted in the hemoperitoneum.

Discussion

Although the possible causes of injury to the diaphragmatic vessels are many and varied, — such as punch biopsy of the liver, erosion by malignancy or abscesses, penetrating wounds of the abdomen and chest, spontaneous or traumatic rupture of congenital aneurysms, and so forth, — the more probable etiologic factor is the needle used during thoracentesis, in view of the frequency with which it is used and the area in which thoracentesis is performed.

Considering that the cases reported indicate a definite danger, we believe that thoracentesis should not be performed until atelectasis is excluded — or unless one is reasonably sure of obtaining fluid, for in both these cases the elevated diaphragm greatly enhanced the danger of vascular perforation.

The diaphragm receives its blood supply chiefly from the phrenic arteries. The superior phrenic arteries supply the superior posterior portion. The inferior vessels supplying the greater portion of the diaphragm arise inconsistently from the aorta or renal or celiac vessels, diverge and run obliquely and laterally on the undersurface of the diaphragm, — the left behind the esophagus and the right behind the inferior vena cava, — and then divide into medial and lateral (or posterior) branches. The former curves forward and anastomoses with those of the opposite side, the musculophrenics and pericardiophrenics. The latter runs laterally toward the lower ribs and anastomoses with the lower intercostal and musculophrenic arteries.

If hemorrhage is present, restoration of blood must be adequate and rapid. In the first case reported here 3000 cc. of blood was given from the time of shock to recovery from anesthesia. One thousand cc. of this was administered under pressure. In both cases 2000 to 3000 cc. of blood was lost.

As this procedure is commonly used in either a diagnostic or therapeutic manner for cases of lung disease, even without the severe hemorrhage and shock such as were found in our cases, these patients might often be poor surgical risks. Therefore, local anesthesia is recommended until the peritoneum is reached. If the diagnosis is confirmed and more relaxation is needed, then general anesthesia may be given.

The incision used was a subcostal one, for it is believed that this allows excellent exposure and can easily be extended to enter the chest cavity if necessary. Nevertheless, surgery was difficult even when this incision was used, as the dome of the diaphragm was markedly elevated and the distance from the incision to the pulsating phrenic artery was approximately 25 cm. This is often the case when the diaphragm is adherent to the chest wall as a result of underlying disease, and this should be borne in mind when instruments are selected for operation. Respirations may be rapid, although not deep, which may further embarrass the surgeon. The anesthetist might aid in decreasing the frequency of excursion[5] by temporarily deepening the plane of anesthesia or by administering curare, as was done in our case, until the injured vessel is repaired.

Severe hemorrhage may not occur if the vessel is small, only partially damaged, located in the muscular area of the diaphragm or pressed on by one of the viscera. For these reasons several such cases of injury to the diaphragmatic vessels have probably escaped attention and have been inconsequential. Nevertheless, as is indicated by the results of the two cases reported here, the danger and diagnosis must be borne in mind and treatment instituted immediately.

Summary

Two cases of severe hemorrhage following injury to the diaphragmatic vessels during thoracentesis are reported. One was diagnosed and treated immediately; the other was identified through reviewing the clinical abstract, including the autopsy record. A case of arteriovenous fistula of phrenic vessels, resulting from the same procedure, is reviewed. Nowhere else have we found this reported as a danger of thoracentesis or of any other operative procedure.

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MEDICAL PROGRESS

SCHIZOPHRENIA AND HORMONES

Some Present Trends: Their Implications and Backgrounds*

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ONE of the most impressive phenomena observed during a recently completed survey[1] of research activities in schizophrenia was the widespread interest in steroid chemistry and adrenocortical function in their application to both clinical and investigative work in this disease. The immediate cause of this interest was obviously the fact that adequate amounts of an adrenocortical hormone (cortisone or Compound E) and adrenocorticotrophic hormone (ACTH) were made available, and had been successfully applied in the treatment of arthritis.[2, 3] The almost miraculous results reported after the use of cortisone and ACTH in arthritis, combined with the psychological effects produced by these substances in the patients, strongly suggested the possibility of similar effects in the treatment of schizophrenia, which was sufficient to arouse the lively interest of most workers in psychiatry. Such a phenomenon is not without its precedents in the history of psychiatry, and particularly in its relation to endocrinology. Thus we find that shortly after the discovery of the role played by the thyroid gland in such conditions as cretinism and toxic goiter there followed a brief period of what amounted to a fad of thyroid treatment in a large variety of mental diseases and particularly in cases of schizophrenia.[4] For several years (the late 'eighties and early 'nineties of the last century) thyroidectomy was performed frequently and even indiscriminately in a large number of cases, until the realization of the futility of such treatment, and the actually injurious results produced in some cases, brought the fad to a conclusion.

At various times after this, similar waves of general interest in the use of endocrine preparations developed in relation to the introduction of such medications as insulin, parathormone, pituitary extracts, testosterone, estrogen and others. In each case, a sudden rise of interest, an unwarranted enthusiasm and finally a restriction of the use of the particular hormone to cases in which its application was warranted by demonstrated deficiency in the normal function of the particular gland followed a definite cycle.

At the present time it is too early to attempt a definite estimation of the real value of either cortisone or ACTH in the treatment of schizophrenia. Investigations of this subject have barely begun; although they are being carried on in many institutions, results on sufficient numbers of patients treated in any one of these places and, what is more important, adequate periods of follow-up study are not as yet available. We will return to this in the following paragraphs, but in order to evaluate

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properly the importance of the investigations currently in progress, it is essential to consider some of the less obvious but probably more important contributions that have been made by studies of hormonal functions in schizophrenia.

It is a well known fact that in endocrinology, just as in other fields of physiologic investigations, the isolation of a biologic substance and its therapeutic application are almost always the result of a long series of basic scientific studies that have preceded an apparently accidental discovery. From the point of view of fundamental research, quite frequently the actual discovery of a therapeutic agent may only be a by-product of such investigations. This is also true of the investigations of the hypophyseal-adrenal system, which have been in progress for a considerable period of time and in the course of which, in addition to therapeutic results, a number of other findings have been obtained that throw considerable light on the general physiology and biochemistry of this system, its relation to and effect on a number of other systems in the body and its role in the function of the individual as a whole and in his physical and psychological adjustment. Most of these contributions were made because of the introduction of new technics of investigation, more adequate means of evaluation and clarification of conditions under which such investigations can be made most effective in their application to the understanding of certain types of maladjustment.

Whatever the outcome of the use of these substances as therapeutic agents in schizophrenia, at the present time it seems quite definite that much greater importance must be attached to the basic results of these investigations and the light they throw on our understanding of this disease. This becomes particularly obvious when we try to evaluate the contributions that have been made to date by a series of investigators since the first attempt to define the relation between endocrinology and schizophrenia began. In each case the impetus given by a new discovery has left in its wake positive knowledge that through the years has been built up into a comparatively systematized understanding of the effects of hormones on the regulation of normal and pathologic personality adjustment. One of the most effective contributions in this direction was made by the group of investigators who for a number of years have been carrying on well organized studies of this subject at the Worcester State Hospital under the leadership of R. G. Hoskins,[5] research director of the Neuroendocrine Memorial Foundation. A short time ago, Dr. Hoskins published an exhaustive report on the results of the investigations of his group in which he undertook an evaluation of the role played by the hormones in the etiology and pathology of schizophrenia.[6] It is interesting to note that in this report he discusses the schizophrenia-hormone relation under the general heading of "the biology of schizophrenia" and presents the disturbances in the endocrine functions as one aspect of the "psychosomatics" of schizophrenia. In keeping with modern concepts of psychiatry, he regards schizophrenia as an expression of a disturbance of the whole human being — his psyche as well as his soma — and comes to the logical conclusion that in order to understand the disease one must be able to grasp the manner in which both physiologic and psychologic factors combine in producing its manifestations. It is obvious, therefore, that the contributions made by students of hormone function can only be effectively applied to the treatment of schizophrenia if and when we come to understand the psychobiologic implications of this interaction.

The scientific validity and practical usefulness of such a concept have been repeatedly demonstrated in a wide variety of pathologic conditions, physical as well as psychiatric. In fact, the subject of "psychosomatic" relations has gained such widespread recognition that it has almost become commonplace. Very few physicians today fail to recognize the fact that emotional stress finds expression in, and may affect pathologically, a variety of somatic functions. The implications of this relation, for instance, in the development of hypertension, allergies of various types, skin diseases, gastrointestinal disturbances and the like are almost generally accepted, particularly when we regard such a process as a psychophysical interaction rather than as a matter of mutual exclusiveness. In other words, it is now fairly well accepted that many of these diseases should be regarded as having mutually supplementary etiologic mechanisms, wherein organically initiated diseases may be exaggerated by emotional stress, just as emotionally conditioned maladjustments may be enhanced by somatic disturbances. It follows, of course, that the various manifestations of these diseases may at times be predominantly due to either organic or psychologic factors, and the recognition of the relative importance of these will guide us in our attempts at prevention and treatment.

It must be appreciated, however, that the bulk of evidence in the development of this concept has come from observations of the so-called psychoneurotic types of personality disturbances, which are characterized primarily by an overreaction to emotional stress, such as hostility, anxiety, worry, tension, frustration and so forth. Until recently few attempts have been made to apply this concept to conditions that manifest the opposite: namely, emotional dullness or hyposensitivity, and the physiologic or hormonal manifestations that accompany them. From the point of view of basic research, schizophrenia, the most characteristic feature of which is the decrease in emotional reactivity, offers the best material for such investigations; at

the same time, from a practical point of view, it is important to appreciate that schizophrenia is one of the most serious and most prevalent of all diseases. When we consider the fact that more hospital beds are occupied by mentally sick patients than by those who suffer from all other diseases, and that almost fifty per cent of psychotic patients belong in the general group classified as schizophrenic, we can readily see both the need of better understanding of this disease and our opportunities for utilizing a vast amount of material in which these conditions can be studied. It must be added, too, that the nature of this disease and its unique course combine with its frequency of incidence to produce an ever-increasing number of victims and a continually mounting drain on social resources. It is a disease that strikes early in life and insidiously, affecting people who are physically and intellectually of at least normal levels — a disease from which, if left to themselves without treatment, very few of the patients will recover spontaneously and for which, until recently, few if any adequate methods of treatment were available. Within the last few years several methods of treatment have been introduced, such as shock therapy, brain surgery, various forms of psychotherapy and, at the present time, the curative possibilities presented by the steroid hormones. In very few such cases do we know the reasons for their therapeutic action; in all of these a better understanding of the psychobiologic relations would help immeasurably in placing them on a rational basis. It is precisely at this point that investigations into the nature of psychosomatic relations and, in regard to the present discussion, the role played by the hormones in the psychosomatic equilibrium, become so important in this field. It is here, too, that recent investigations, and others at present in progress, dealing with the better understanding of the chemical nature of the hormones, their relation to the central nervous system and other organs and their effect on human adjustment, have become so important and have superseded the more immediate concern with specific therapeutic procedures.

It is not possible here to undertake a complete review of all the contributions that have been made concerning functions of the different glands of internal secretion and the evidences of disturbances of each in persons suffering from schizophrenia. I might again refer to the publication by Hoskins[6] in which a summary of conditions up to 1946 is given, but I should prefer to concentrate here on several trends that have developed within the last few years and are still in progress, and discuss their implications as they are related to the thesis that we have developed so far.

Schizophrenia, in spite of the fact that it has probably existed all through the history of mankind and has been known and investigated as a distinct disease for almost one hundred years, is still a somewhat amorphous concept. Indeed, it is probably true that the vast number of persons diagnosed as schizophrenic really represent a group of diseases rather than one single entity. Within it we have variations in almost every conceivable aspect, including the etiology, onset, duration, course, prognosis, characteristic symptoms, presence or absence of accompanying physical variants, constitutional predispositions, probability of reaction to certain types of treatment and so forth. Obviously there must be some central factor, no matter how general, that is more or less universally present in these cases to justify a common diagnosis. Such a feature is represented by what we might designate as a "withdrawal" reaction. By this, we mean that these patients are all characterized by psychologic and social withdrawal from the competitive struggle for adjustment; they seem to have retired into a world of their own. They seem to have surrounded themselves by a wall of indifference to the stimuli from both external and internal environment that in other persons serve as incentives to the effort of adjusting to life stresses. It is in this respect that they seem to range themselves in relation to the general population at one end of the spectrum of adjustment, at the other end of which we find the bulk of the so-called psychoneuroses. For whereas the latter show hypersensitivity to emotional stress — a higher than normal reactivity to such emotions as fear, guilt, frustration, pain and the like — the schizophrenic patient shows the opposite: a lack of or, at least, an attenuated reactivity to such stress.

It is important to emphasize here that this lowering of emotional reactivity has been observed to coexist with a similar lack of reactivity to physical stresses; here, too, they seem to be behaving in a manner opposite to that of the psychoneurotic patient. A number of such observations have been made empirically over the years. Few, if any, schizophrenic patients suffer from allergies, hyperthyroidism, hypertension, angina, peptic ulcer or migraine.[5] The psychosomatic studies of these illnesses have shown the importance of overreaction to emotional stress in their development, and at the same time have demonstrated the role played by hormonal balance and general homeostasis in emotional reactions. It was considered logical, therefore, to investigate the state of reactivity of schizophrenic patients to hormonal substances; the results obtained so far justify this trend of thought. Schizophrenic patients to whom thyroid was administered in such doses as fifteen to eighteen grains per day for months showed very little effect, in terms of either emotional or physiologic reactions; where such reactions were found they were certainly less marked than those to be expected in an average person.[7] A similar failure in adequacy of reaction was found in regard to insulin. A number of observers have described a marked resistance

to insulin in schizophrenic patients and have demonstrated increase in anti-insulin substance in these patients.[8] Similar reactions were found in the use of other substances, such as testosterone. The most important lead in this direction was furnished by the results of a long series of investigations of adrenocortical function and the demonstration of its role in general adaptation and reaction to stress.[9] For several years a number of investigations have been in progress on this system in various forms of mental disturbances. Perhaps the most systematic study of this mechanism in the case of schizophrenia was made by the group working at the Worcester Foundation for Experimental Biology under the direction of Drs. Hoagland and Pincus. Utilizing a number of indices of adrenocortical function in terms of activation of the end organs, including the urinary output of potassium and sodium, uric acid, 17-ketosteroids, neutral reducing lipids and changes in the number of circulating lymphocytes, these observers studied a number of normal subjects, schizophrenic patients, and some psychoneurotic patients, all of whom were subjected to certain uniform situations of stress. The stresses used consisted of the target-ball frustration test and the operation of a pursuit meter for one hour. These were supplemented by studies of the effects on the indices of the administration of adrenocortical extract and of pituitary adrenocorticotrophin. This study was based on the fact that when a normal person is placed under stress, physical or psychological, evidence is manifested by the above indices of an increased function of the adrenal cortex in response to the stress situation.[10-13] Some observers have found that in some psychoneurotic patients, particularly in anxiety states, an accentuation of the normal reaction can be demonstrated.[14] In the case of schizophrenic patients, however, the Worcester group was able to demonstrate a "highly significant failure of normal adrenal stress responses as compared with controls."[15] This failure to respond either adequately or at all was not seen in all patients diagnosed as schizophrenic. Actually a little over three quarters of the patients manifested this hyporeactivity, which is of particular interest in view of the fact that schizophrenia cannot be regarded as a single entity, even clinically; it is possible that these investigations may be of help in bringing about a more exact delineation of subgroups and consequently more clear-cut indications of the applicability of therapeutic methods.

The application of these findings in the search for further understanding of the pathology of schizophrenia and for effective therapeutic methods depends largely on our ability to determine the specific part of the pituitary-adrenal mechanisms that is responsible for the failure to respond. Logically, the findings reported could be due to: failure of the end organs to respond to an adequately functioning adrenal cortex, failure on the part of the adrenal cortex itself and failure of the pituitary gland to provide the necessary stimulation in terms of ACTH. The first of these possibilities is definitely excluded by the fact that when adequate amounts of adrenocortical extract (ACE) are administered, the reaction of the end organs is the same in both schizophrenic and normal subjects. This, however, is not the case when ACTH is administered, since about three times as much of this substance is required to evoke the same over-all quantitative response in schizophrenic patients as it does in normal subjects, and qualitative differences in the response are manifested.[15] This indicates that the reasons for failure to respond to stress are to be looked for either in an altered threshold of the adrenal cortex or in the complex mechanism involved in the process of adrenal hormone release in response to both endogenous and exogenous ACTH. These considerations must also be kept in mind in evaluating recent reports of other observers,[16] who found that injections of epinephrine and the use of insulin and electric-shock treatment produced lymphocyte responses in schizophrenic patients that were similar to those found in normal persons. Pincus and Hoagland[15] have presented cogent criticisms of the use of these forms of stimulating agents of the pituitary-adrenal cortical system when compared to other forms of stress.

This also brings us to the discussion of the therapeutic results of the administration of either cortisone or ACTH in the treatment of schizophrenia. It has been stated above that at the present time the results are not conclusive. Some reports maintain that temporary beneficial effects are produced in some cases, particularly where states of depression are present.[17] Others indicate that satisfactory therapeutic effects can only be produced when these substances are used in conjunction with other methods of treatment, such as electric shock, which in themselves were not successful. Still others find that in most instances where beneficial effects are produced they are temporary, and in other cases no positive results are obtained. In evaluating the implications of these therapeutic attempts we must, however, keep in mind that the number of patients treated so far is not sufficient, and that the follow-up period is not long enough to permit conclusive statements. Furthermore, the failure to obtain results with the few steroid substances available is no indication that others may not be found that will be more effective. Finally, it would seem logical to expect that the development of a positive, rational method of therapy must await further clarification of the exact mechanism of the disturbance.

Closely related to these investigations, and in fact forming an essential part of them in terms of supporting the general conclusions, are the results of studies of the disturbances in carbohydrate

metabolism in schizophrenia. The fact that the function of the pituitary-adrenal system is closely related to carbohydrate metabolism has been demonstrated by a number of investigators. Thus Conn and his co-workers[18] have reported temporary diabetic states induced in normal persons by large doses of ACTH and have demonstrated that the diminished glucose tolerance following multiple injections of ACTH is associated with diminished blood glutathione levels. Kass and his co-workers[19] have also reported the development of glycosuria after treatment with ACTH. At the same time it was found by other investigators[20] that the administration of large doses of glucose serves to stimulate adrenal-cortical activity in normal persons in the same manner as found in reaction to stress situations. This was shown by the fact that the various indices used in the evaluation of the effect of other stress situations on the adrenal cortex manifested the same changes after ingestion of glucose. A number of investigators have therefore undertaken studies of glucose tolerance in patients suffering from schizophrenia, comparing them with similar studies in normal people and psychoneurotics. Freeman[7] and his associates report the results of a series of such investigations with the following findings: Using the Exton–Rose method of determination, they found that normal persons under basal conditions show in the majority of instances a rise in blood sugar at the end of the first half hour and a fall at the end of the second. Similar findings are reported in cases of psychoneuroses. In schizophrenia, however, they found in the majority of cases a continuation of the rise of the blood-sugar level at the end of the second half hour. At the same time, lymphocyte counts that in normal subjects and in psychoneuroses showed a reversed curve as compared with the blood sugar (namely, a fall in the lymphocytes at the end of the half hour and a rise at the end of the hour) were different in schizophrenic patients. Similar differences were obtained in determinations of uric acid and potassium. It is of particular interest to note that a parallel study of the psychologic findings in these patients shows that the abnormal glucose tolerance is most likely to be obtained in cases in which Rorschach studies indicate the presence of psychic disturbances, and that in some patients who were successfully treated the amelioration in the clinical picture frequently was accompanied by a return of the glucose tolerance to a more nearly normal curve.[21]

Other observers have also found more or less similar disturbances of carbohydrate metabolism in schizophrenic patients,[22] and reference has previously been made to the work of Meduna[8] and his associates, who have reported the presence of high quantities of anti-insulin substance in the blood of a certain group of schizophrenic patients. Actually, these observers have attempted to divide the clinical manifestations of schizophrenia on the basis of their glucose-tolerance reactions and accompanying psychotic manifestations.

Another facet of this complex problem is represented in a series of important investigations dealing with the study of the autonomic nervous system in schizophrenia. Funkenstein and his associates[23, 24] have reported the results of a number of investigations in this field, and some of their studies are still in progress at this time. They deal primarily with observations of the reactions of schizophrenic patients to adrenergic stimulation (intravenously administered epinephrine) and parasympathetic stimulation (intramuscularly injected mecholyl). In measuring these reactions they utilized responses of the cardiovascular system, such as cardiac output, peripheral resistance, pulse and blood pressure; they also made determinations of blood sugar, central-nervous-system reactions, effects of acetylcholine and release of ACTH. These studies were originally started for the purpose of finding, among other things, criteria for the prediction of clinical results in the treatment of schizophrenic patients. Their observations, however, have led them to broaden their base of inquiry to more general considerations, such as the attempt to clarify the basic difference among the various groups in this disease, the relation of the physiologic disturbances to the psychologic manifestations and the possibility of finding the nature of the relation of the autonomic-nervous-system disturbances and dysfunctions in other systems. On the basis of their studies so far, they are able to classify schizophrenia into seven types, which are different psychologically, physiologically and prognostically. They have studied very closely three of these groups, which are of most frequent occurrence and make up the great bulk of schizophrenic patients. One of these groups is characterized clinically by the fact that the patients recover more quickly, either spontaneously or after electric shock; physiologically it is characterized by an excessive secretion of an epinephrine-like substance. When they recover after treatment, these patients show evidence of oversecretion of acetylcholine, which has the effect of counteracting the oversecretion of adrenalin. A second group shows evidence of oversecretion of a nor-epinephrine-like substance. These patients do not respond well to electric shock, but about fifty per cent of them respond to insulin. Finally, a third group represents patients who rarely recover. Psychologically, they show a marked loss of abstract thinking that may indicate serious physiologic disturbance of the higher centers. The disturbances of the autonomic nervous system in these cases suggest a mechanism closely related to that described as "release" of the autonomic nervous system from higher control. They show low blood pressure and high reaction to adrenalin but no increase in blood pressure to psychologic stimuli.

Of interest in relation to the second group is the fact that nor-epinephrine, as contrasted with epinephrine, shows failure to stimulate the anterior pituitary gland to secrete ACTH; acetylcholine does not counteract its effects. It has a specific influence on the cardiovascular system that is quite different from that of epinephrine, and has little effect on carbohydrate metabolism in contrast to the profound changes brought about in this system by epinephrine.

Recently these workers have studied a series of patients suffering from asthma.[25] They have found that a number of such patients have subsequently developed schizophrenia and that when this disease was established the asthmatic attacks ceased during the duration of the psychosis. When they recovered from schizophrenia, asthmatic attacks recurred. Physiologically it was of interest to note that these changes in the patients' clinical pictures paralleled changes in their autonomic nervous systems. Their reaction to epinephrine and mecholyl was entirely different in the asthma-free psychotic phase from the reactions obtained in the nonpsychotic asthmatic periods.

The results of these investigations are of great significance for a number of reasons. In the first place, they tend to support the conception of schizophrenia as a psychosomatic disturbance. This is supported by the positive correlation between psychologic symptoms and specific dysfunctions of the autonomic nervous system, as well as by the fact that changes in the course of the disease are concomitant with alterations in the autonomic response. Secondly, their studies of schizophrenia in asthmatic patients substantiate the idea expressed above that psychosomatic disturbances may be expressions of pathologic conditions at either end of the spectrum of psychologic and physiologic reactivity. Thirdly, they point to new potentialities for establishing more valid criteria of diagnosis and for the development of rational methods of treatment.

The investigations reported above represent important trends currently in progress in the attempt to clarify the relations between hormonal functions and the clinical disturbances grouped under the name of schizophrenia. Studies of the functions of other glands of internal secretion have continued; some of the results are closely related to the studies here discussed, as would be logically expected in view of the close interdependence that exists among the various representatives of the chain of endocrine glands. However, findings that have been discussed in the investigations of the pituitary-adrenal cortex system, the carbohydrate metabolism, and the adrenal medulla-autonomic nervous system suffice to indicate the importance of such work. From a practical viewpoint they are of value in providing a beginning for the search for therapeutic procedures. In a general way, however, these investigations present even more important implications. The fact that all these studies tend to isolate separate groups, within the whole field of schizophrenia, each group characterized by more or less specific physiologic disturbances, may in the future prove of great importance in placing research in this disease on a more scientific basis. They suggest the possibility of different etiologies and of different types of reactions to the stresses of life. Attempts at both prevention and treatment will undoubtedly profit from investigations of this type. For if the differentiation can be more clearly delineated, we will no longer be baffled by the frustrating experience of claims and counterclaims in regard to effect of specific therapies as they are reported by various observers.

Finally, the most important aspect of these contributions, so far as the fundamentals of the nature of schizophrenia are concerned, is that they provide a basis for better understanding of the relation between the clinical-psychologic manifestations and the physiologic mechanisms involved. They point the way toward the establishment of a sound psychosomatic concept of schizophrenia, in which the vicissitudes of sociopsychologic problems and their impacts on physiologic functions can be regarded as manifestations of the same process: the general adaptation of man to the stresses of life.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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CASE 37241

PRESENTATION OF CASE

A three-month-old white male infant entered the hospital because of paralysis of the legs.

The child was born in the thirty-seventh week of gestation by frank breech presentation. Except that the legs were markedly flexed, no further details of the birth were available. Although at the time of birth it was believed that the legs moved and responded to pain, it was shortly afterwards observed that there was some impairment of leg movements. X-ray films of the hips taken at this time were normal. It was also noted that since birth there had been a continual dribbling of urine. About one and a half months before admission, it was found that the patient cried whenever he was lifted by the legs for changing diapers. Whenever he cried his body "turned purple from the lower abdomen down, instead of the normal red." His physician found at that time that there was a complete flaccid paralysis of both legs. An attempted myelogram at an outside hospital was unsuccessful. The child's state remained essentially unchanged to the time of admission except for constipation; previously stools had been "loose."

In other respects the child had been well. He fed and gained weight well. The family history was unremarkable.

On examination, the infant was well developed and well nourished and appeared alert. There was a small umbilical hernia and a small, easily reducible right-inguinal hernia. There was a slight scoliosis of the spine, convex to the left in the lower thoracic and upper lumbar region, and some prominence of the left flank. General physical examination was otherwise normal. On neurologic examination the cranial nerves and the arms were normal and respiratory movements were unimpaired. There was less tone in the abdominal musculature below the umbilicus than above it. The legs were flaccid and totally paralyzed. Tendon reflexes were present and normally active in the arms but absent in the legs, and the abdominal reflexes were absent. The plantar reflex was absent on the right, flexor on the left. The tone in the anal sphincter was good, but there was dribbling from the bladder. There was no response to pain in the legs, but the patient cried occasionally when pricked between the groins and umbilicus and invariably when pricked above the umbilicus. Below the umbilical level the skin was drier than elsewhere and somewhat mottled. Skin-resistance measurements showed no differences between the lower and upper halves of the body.

The temperature was 98.6°F., the pulse 100 and the respirations 30.

Urinalysis was normal. Examination of the blood revealed a hemoglobin of 9.8 gm. (11.8 gm. after transfusions) and a white-cell count of 6800, with a normal differential. The nonprotein nitrogen was 17 mg. and the total protein 5.2. gm. per 100 cc. The prothrombin time was 14 seconds (normal, 17 seconds). X-ray films of the spine showed a smoothly rounded soft-tissue density on the right side of the vertebral column extending from the ninth thoracic to the second lumbar level (Fig. 1). There was slight scoliosis of the lumbodorsal spine, convex to the left, with the apex of the convexity at the tenth to eleventh thoracic vertebra. Lumbar punctures between the third and fourth lumbar vertebras and the fifth lumbar and first sacral vertebras, performed for myelography, yielded xanthochromic fluid that rapidly became bloody. About one-fourth cc. of Pantopaque introduced into the vertebral canal did not move.

On the fifth hospital day an operation was performed.

Differential Diagnosis

Dr. Clement A. Smith*: This is a not very long but sometimes rather vague story. It is especially vague about the exact time of onset, but it is seldom very easy to find out exactly what a baby's status was in the immediate postnatal period. The obstetrician has two patients to take care of, and the baby is assumed to be all right if he is breathing and crying and has good color. Moreover, since one does not expect very much from a baby at birth in the way of moving around, it is always difficult to decide how sharp the onset of a paralysis is. Obviously the baby seemed to have motor trouble before he left the hospital. The fact that there had been continual dribbling of urine from birth apparently dates the lesion to the time of birth or before.

Figure 1.

Here was a baby delivered by breech and in trouble right away. The symptoms of immediate bladder weakness and presumably early leg weakness could have been produced by a cord lesion, and even the turning purple of the lower abdomen when he cried may have been related to vasomotor dilatation with stagnation of blood such as could have occurred under those circumstances and would have been more marked below the level at which sympathetic innervation had been involved. Anyone who has had the privilege of being associated with Dr. Bronson Crothers and has worked in a lying-in-hospital would think at once of a spinal-cord injury. Up to the time the baby was admitted to this hospital, that diagnosis was acceptable. Nothing was clearly against it, and several things were in favor of it — especially the breech delivery. It has been our sad experience that children can have spinal-cord injuries as a result of traumatic delivery. The physicians who were caring for the baby also thought there was something wrong with the cord, as they attempted a myelogram, which was unsuccessful.

Although many babies have umbilical and inguinal hernias, their presence in this baby makes me wonder if there were not unusual weakness of the abdominal muscles. The neurologic findings show that the lesion that I presume was affecting the cord was probably about at the lowest thoracic segment. The note that the plantar reflex was absent on the right and flexor on the left only means to me that with any but a very cleanly produced experimental transection of the cord all sorts of dissociations of neurologic signs may be produced. The varied response to pinprick also gives indication of a diffuse rather than a sharp level of the ceiling of the lesion. The dryness and mottling of the skin below the umbilicus would be in keeping with changes of sympathetic innervation below the rough level stated.

The 9.8 gm. of hemoglobin was not below the amount found in many quite normal three-month-old infants. A white-cell count of 6800 was perfectly normal. One wonders why the physician measured the serum protein. Most probably it was done because it was thought that a mass somewhere near the kidney may have been interfering with renal function, but a pyelogram was not done. The prothrombin time was near enough to normal to rule out any excessive tendency to bleed in this baby.

Perhaps Dr. Hanelin might point out the x-ray findings. Here we come upon something that is very significant.

Dr. Joseph Hanelin: There is evidence of a soft-tissue mass that lies to the right of the lower thoracic spine and extends from approximately the ninth thoracic to the first lumbar vertebra. Not described in the protocol is a vague density that lies posteriorly on the left at the same level, very likely continuous with the density that lies to the right of the spine. There is also a suggestion of a mass lying in the left upper abdomen. All these masses may be confluent. The kidneys and the individual abdominal viscera are not very well defined in these films (Fig. 1).

Dr. Smith: You do not see any calcification in that part of the lesion?

Dr. Hanelin: No; I do not see any calcification.

*Associate professor of pediatrics at the Boston Lying-in Hospital, Harvard Medical School.

DR. SMITH: Are the bodies of the vertebras all normal, so far as you can tell?

DR. HANELIN: There are no obvious destructive changes.

DR. SMITH: Were all these films taken on the same day?

DR. HANELIN: They were taken twenty-four hours apart.

DR. SMITH: There is an unusual degree of gas in the patient's stomach, beyond the degree you might see normally. One wonders if there may have been some obstruction along the upper jejunum and also possibly some decrease in peristaltic movement associated with the constipation on the basis of innervation disturbance.

Where I had one mass I now have two, and that worries me a good deal, but it practically forces me to abandon the idea of trauma. It would have been difficult for oozing from accidental damage to the spinal cord with tearing of the dura to result in the escape of enough blood to produce a visible mass, let alone two masses. And what would hold the blood in the form of a mass? It would dissect down through fascial planes. The idea of trauma goes out the window at that point.

The lumbar puncture below the level of the lesion gave xanthochromic fluid, which would be expected below a compressive lesion, and the fluid rapidly became bloody. That was against trauma occurring at birth, as I cannot believe that there would still have been oozing at three months. Pantopaque was introduced but did not move. Is that shown in one of these films?

DR. HANELIN: Yes; there is a tiny amount without any characteristic form.

DR. SMITH: I think this child had either a neoplastic mass or a cord injury. For reasons I have stated and won't elaborate on further I am inclined to put the cord injury in pretty low second place. If there was a tumor, what was it? Seemingly, if it originated inside the dura or inside the vertebral canal it must have grown outward and produced relatively tremendous growth outside. I think it much more likely to have been an epidural tumor or a tumor arising adjacent to the vertebral column, presumably retroperitoneally. A retroperitoneal tumor apparently pushing the spine away from it is somewhat hard to understand, since that does not usually happen; usually the abdomen or the flank is pushed outward. On the basis of statistics, which usually is the most helpful approach, it is more likely to have been a neuroblastoma, since these occur in the newborn period and very commonly in this site. In origin, these tumors are — but why should I tell you what they are, since Dr. Mallory will tell you better than I could if I am right. Such tumors have plenty of opportunity to arise from this particular region; they can and often do work their way along nerve trunks into the inside of the vertebral canal; they may press on the cord, and sometimes even destroy it; and they also may grow beyond the vertebral canal and down the other side.

My first choice, then, would be neuroblastoma. By breaking down, which commonly happens, this tumor could have produced the blood that was found in the spinal fluid before operation. This tumor seems to have grown not only into but through the vertebral column. If it was not a neuroblastoma but was still a tumor, as it seemed to be, it must be a dermoid or one of the more rare neoplastic conditions. My second diagnosis is that it was some other form of tumor, and my third is that it represented the consequence of cord injury at birth.

CLINICAL DIAGNOSIS

Spinal-cord lesion: ?birth injury with hematoma, ?abscess, ?tumor.

DR. SMITH'S DIAGNOSIS

Neuroblastoma, arising retroperitoneally, with invasion of vertebral canal and compression of cord.

ANATOMICAL DIAGNOSIS

Neuroblastoma (in newborn), arising retroperitoneally, with invasion of vertebral canal and compression of cord.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Dr. Selverstone, will you tell us how opinion ran in the hospital preoperatively and what you found at your exploration?

DR. BERTRAM SELVERSTONE: One of the reasons for the abdominal distention on admission may have been the child's airplane trip from South Carolina on that day.

The protocol covers the preoperative course quite well. At operation, after laminectomy, the internal periosteum of the laminas was found to be markedly distended by a red fleshy tumor mass, rather granular in appearance, that extended up to about the ninth thoracic segment and down to about the second lumbar segment, just as did the paravertebral mass seen in the x-ray films. The tumor was extradural. It had displaced the dural sac anteriorly and to the right, where it was crowded against the right anterior part of the vertebral canal. On frozen section the tumor was a neuroblastoma. Postoperatively the patient was relieved of pain when the lower limbs were raised to change his diapers. Otherwise his condition remained the same. The baby went home on the sixth postoperative day. As much of the tumor as was accessible was removed in the hope of relieving the baby's pain.

DR. JAMES C. WHITE: Did you see any tumor that had grown out through the intervertebral foramina?

DR. SELVERSTONE: Yes; you could see that it was continuous within the intervertebral foramina.

It crowded into every possible corner of the canal. One could not be certain that it extended outside to become confluent with the mass, but I assume it did so.

DR. MALLORY: As Dr. Selverstone has stated, it was possible to make a diagnosis of this tumor on frozen section, which was readily confirmed by the paraffin sections. It was a reasonably characteristic neuroblastoma. These tumors consist of uniform small cells of about the size of lymphocytes although with entirely different character. In a good preparation it can be shown that the cells are slightly pear-shaped, and at one end a filament is produced. This filament is extremely tenuous and very difficult to stain. There is a tendency for the cells to be grouped in small circles with the fibril oriented toward the center; the name "rosette" has been given to that appearance, but I think the term has been unfortunately overemphasized, as many neuroblastomas show no well defined rosettes and a good many other tumors show pseudorosette formation, which can be considerably more dramatic than the real thing. It was not possible, of course, from the point of operative approach to this tumor, to demonstrate where it was primary. It is rather unlikely that it was primary in the spinal canal. The commonest locations are the medulla of the adrenal gland, the ganglia of the sympathetic nervous system and of course the retina, which I think is adequately ruled out by the clinical examination in this patient.

DR. JACOB LERMAN: Is the invasion by extension or by metastasis?

DR. MALLORY: It can be either, and frequently is both. I am not sure we can say with certainty in this case, although I think it is very likely that it would extend into the spinal canal along the nerve roots. Was that your impression at the time of operation, Dr. Selverstone?

DR. SELVERSTONE: Yes, it was.

DR. MALLORY: Is there anything else you would like to know, Dr. Smith?

DR. SMITH: I should like to ask about the prognosis and the further care arranged for the child. Occasionally we see rather surprisingly good results from the radiologic attack on these tumors. In an occasional one, which stands out more than it should because it is such an oddity, the tumor apparently outgrows its own blood supply and dies, so to speak, resulting in an apparently spontaneous cure. We have had at least one such instance — I think two. We have had about 25 per cent of cures in neuroblastoma, sometimes under extremely unfavorable circumstances, and by no means always on the basis of complete surgical removal of the tumor. One of the things that Dr. Sidney Farber insists upon is that an attitude of hopelessness is not justified even under what look like extremely hopeless circumstances.*

DR. SELVERSTONE: Because the baby's lower limbs and bladder were completely paralyzed and had been so for over three months, no extreme measures were recommended. It was suggested to the pediatrician who sent the baby here that x-ray therapy should be used if the baby ever again appeared to be in pain. In view of your comments, however, it might be well to revise that advice and to suggest that he decide whether the remote chance of long-term therapeutic effect from x-rays might not be taken into consideration.

DR. SMITH: You think the cord was destroyed?

DR. SELVERSTONE: That would be my impression — after three months of complete paralysis.

*Wyatt, G. M., and Farber, S. Neuroblastoma sympatheticum: roentgenological appearances and radiation treatments. *Am. J. Roentgenol.* 46:485-495, 1941.

CASE 37242

PRESENTATION OF CASE

A forty-four-year-old serviceman entered the hospital complaining of attacks of pain in the stomach.

The patient, who had been in good general health, received a dull blow to the epigastric region twenty-one months before admission. The blow was sufficiently severe to knock him down but not to cause loss of consciousness or any other immediate sequelae. Three months later he began to have attacks of epigastric pain radiating around the abdomen into the back and lasting from a few hours to several days. The pain was sometimes dull in character and sometimes squeezing. It was not apparently related to meals, time of day or activity. The patient was frequently nauseated during attacks and on a few occasions vomited material resembling bile.

Fifteen months and again five months before admission the patient was studied at a community hospital, where repeated gastrointestinal and gallbladder series were said to have been negative. On the second of these admissions the blood sugar was found to be elevated and he was placed on 20 units of protamine zinc insulin a day, which he continued to take up to the time of admission. A few weeks before entry further x-ray studies were said to have shown distortion of the superior edge of the first part of the duodenum, and further hospitalization was advised.

The patient had no weight loss during his illness. His appetite was good except during the attacks of pain. There had been no change in bowel habits or character of the stools. He denied any alcoholic intake for three months before admission. Prior to this he had consumed two or three bottles of beer and two highballs a day. One sister had died in diabetic coma at the age of thirty-two.

Physical examination revealed a well nourished and well developed man in no distress. The only unusual finding was a slightly tender, lobulated mass in the epigastric area that moved on respiration.

The temperature, pulse and respiration were normal. The blood pressure was 105 systolic, 70 diastolic.

Urinalysis was unremarkable. Examination of the blood revealed a hemoglobin of 13.4 gm. and a white-cell count of 7400, with 59 per cent neutrophils, 29 per cent lymphocytes, 7 per cent monocytes and 5 per cent eosinophils. One stool specimen was guaiac negative. The blood Hinton test was negative. The blood sugar was 103 mg., the amylase 30 units and the alkaline phosphatase 3.3 units per 100 cc. The prothrombin time was normal and a gallbladder series showed a good concentration of dye without evidence of included calculus. The gall bladder diminished in size after a fatty meal.

On the fourth hospital day an operation was performed.

Differential Diagnosis

Dr. Briant L. Decker*: In summary, this forty-four-year-old man, who had previously been well, had a rather severe blow to the abdomen and soon afterwards developed attacks of pain in the epigastrium that radiated around the abdomen to the back and were occasionally accompanied by nausea and vomiting. He had diabetes. The only finding on physical examination was a tender lobulated mass in the epigastrium that moved with respiration. The laboratory tests were normal and apparently, with the exception of one gastrointestinal series, the x-ray films were normal. This examination was said to show irregularity of the superior surface of the first portion of the duodenum.

May I see the films?

Dr. James J. McCort: The outside films are not available. On the Graham test made in this hospital, there is fair concentration of dye in the gall bladder. The gall bladder is not dilated and no stones are seen. That is about the limit of the information from this examination.

Dr. Decker: I shall have to follow the protocol from here on. I believe that this mass was most likely located between the stomach and the liver. In the first place, it moved with respiration; in the second place, it apparently caused some irregularity of the superior surface of the first portion of the duodenum. Its consistence was not described, nor was its size. And one has no chance of determining anything about its size from these x-ray films. Of course, in trying to determine its nature it is important to decide its origin. The fact that it moved with respiration is strongly suggestive that the site of origin was the liver. The possibility of its being gall bladder, I think, is pretty well ruled out by its position and by the fact that the gall bladder filled. This coincides with the findings in the films done outside. In considering the question of the types of lesions that may be attached to the liver, one thinks of echinococcus cyst. I am sure if such a cyst had been likely the abstract would have included information about this man's geographic origin or his travels. He was said to have been a serviceman, however. An echinococcus cyst is usually solitary and smooth. Of course, it may be large. There was no eosinophilia. I think echinococcus cyst is rather unlikely. Then there is the question of a congenital cyst of the liver. Congenital cysts are usually small and multiple, although occasionally they may be large and may be associated with polycystic disease of the kidneys. There was no evidence of that.

Could it have been a mesenteric cyst? These are, of course, rare, and they almost always occur before the age of thirty. They are usually in the midabdomen, are usually freely movable and are not lobulated. Although I think it is possible that this patient might have had such a cyst in the gastrohepatic omentum, it seems to me the mass most likely had a retroperitoneal origin in or adjacent to the pancreas and was therefore probably a pancreatic cyst.

In general there are three types of pancreatic cysts. Retention cysts are apparently due to chronic partial obstruction of ducts and are small. I do not think I need to consider those. The cystic neoplasms, — cystadenomas, papillary cystomas and so forth, — are true tumors; they may be multilocular. I think that a cystic neoplasm is a good possibility in this case. However, there are usually more severe constitutional symptoms— pain, loss of weight, nausea, vomiting and so on. This patient had all these symptoms except loss of weight, and his general health had been good.

The third type, the pseudocyst, is the most common pancreatic cyst. They are usually single and frequently are large but usually not lobulated, as this was said to be. These cysts are not in the pancreas but in the lesser peritoneal sac. They are caused by the collection of blood or the products of pancreatic secretion and digestion. The majority of these cysts follow previous attacks of acute inflammation — acute pancreatitis — but about 30 per cent follow trauma. You remember that this patient did have an episode of fairly severe trauma. The cyst is usually located between the stomach and the liver behind the gastrohepatic omentum or between the stomach and the colon in the layers of the gastrocolic omentum. These cysts may also be found in other regions, but those are the two most common locations. I believe that the mass found in this patient was that sort of cyst — a pseudocyst of the pancreas.

Of course there are other types of cysts that might be considered. Dermoid cysts are extremely rare in this particular region. Lipoma is very slow-

*Assistant physician, Massachusetts General Hospital.

growing, is fixed and may become very large. Lymphoblastoma seems unlikely because of the normal blood picture, lack of fever and lack of a palpable spleen.

It is my opinion that this was a pseudocyst of the pancreas.

DR. JOHN T. QUINBY: May I ask Dr. McCort if there is any evidence of enlargement of the liver in the x-ray film?

DR. MCCORT: No enlargement is apparent.

DR. JOHN B. STANBURY: Can you follow the liver edge perfectly well? Is there any interruption of it?

DR. MCCORT: I cannot follow it very well in these films because of the presence of a large amount of feces in the colon. There is no interruption of it to indicate the presence of tumor.

DR. MARSHALL K. BARTLETT: We had the opportunity of feeling this mass, but we did not do as well as Dr. Decker did in making the correct preoperative diagnosis. It was a sizable mass. One could see a protrusion of the epigastrium as the patient lay in bed. We thought that the mass was probably in or attached to the liver. Our differential diagnosis centered between a pancreatic cyst — presumably a pseudocyst — and metastatic disease in the liver. In favor of the former were the reasons that Dr. Decker has given — the trauma, the recurrent attacks of pain, the development of diabetes, which is not usually but occasionally present with these pseudocysts, and the position of the mass. One thing that deterred us from the diagnosis of pancreatic cyst was that it seemed to us that any cyst of this size arising in the pancreas and presenting above the lesser curvature ought to displace the stomach so that it would be recognizable by x-ray examination. The last x-ray examination was done before admission by a very keen x-ray observer. He noted the distortion in the superior portion of the duodenum and raised the question of ulceration in that region. We believed from feeling this mass that it was more likely to be metastatic disease in the liver. Against that was the man's good general condition. He was in excellent health between attacks and had lost no weight.

CLINICAL DIAGNOSIS

Carcinoma of pancreas with metastases to liver.

DR. DECKER'S DIAGNOSIS

Pseudocyst of pancreas.

ANATOMICAL DIAGNOSIS

Pseudocyst of pancreas.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Dr. Bartlett, will you tell us your findings at operation?

DR. BARTLETT: When we opened the abdomen it was apparent that what we had been feeling was the liver. The liver surface was perfectly smooth, so any irregularity that we felt was entirely imaginary. When we lifted up the right lobe of the liver there was a large smooth-surfaced cyst of a bluish color with a relatively thick wall occupying all of the region between the lower surface of the liver and the lesser curvature of the stomach. The cyst involved the retroperitoneal structures in such a way that we thought if it was a neoplasm it was totally inoperable. The pancreas seemed to be firmly attached to the lower border of the cyst. It is interesting that the pancreas from that point out to the tail was firm, diffusely involved and much harder than normal. However, it did not feel like cancer. The gall bladder was normal. It was possibly displaced to the right but otherwise not remarkable. We could find nothing else abnormal in the abdomen.

We opened the cyst and evacuated about 800 cc. of tan-colored fluid, which obviously contained old blood. A biopsy of the cyst wall was taken and a frozen section showed no evidence of neoplasm. After the evacuation, the cyst wall collapsed and the whole mass was a good deal smaller than it had been. Then the question came up whether to drain the cyst externally or to anastomose it to some part of the gastrointestinal tract. As you all know, some of these pseudocysts have been treated by attaching them to the gastrointestinal tract. We have not had much experience with that in this hospital. I do not see how one can fail to contaminate the cyst cavity if one deals with it in this way. It was not possible to bring it out to the peritoneum, to marsupialize it, so we simply took a large catheter, sewed it in and closed the cyst wall around it, much as you would drain a gall bladder. The cyst fluid was analyzed. It contained 140 Russell units of amylase and 20 cc. (normal blood serum under 2 cc.) of lipase. Since operation the patient had drained very small amounts — not more than 100 cc. the first day or two and now only 20 to 30 cc. a day — from the catheter. The diabetes is about the same; the blood sugar is essentially normal on 20 units of protamine zinc insulin a day.

DR. MALLORY: The fragment of the cyst wall that we received for examination consisted only of fibrous tissue with a moderate infiltration of inflammatory cells. There was no epithelial lining such as one would expect with a retention cyst or, of course, with a neoplastic cyst. Therefore, it seems to be characteristic of a so-called pseudocyst of the pancreas.

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IS IT BEING OVERDONE?

In a recent address before the New York Academy of Medicine, Finland* reviewed the many prophylactic and ancillary uses of antimicrobial agents. It is quite obvious from his survey that sulfonamides and the antibiotic agents, when intelligently applied, have proved to be extremely useful and of enormous value, both in isolated individuals and in large groups, as preventives of certain specific infections such as meningococcal meningitis and gonorrhea. They have also probably reduced the incidence of infectious complications in such situations as large-bowel and genitourinary surgery, and they may have prevented the occurrence or recurrence of subacute bacterial endocarditis in patients with congenital or rheumatic heart disease.

*Finland, M. Present status of antibiotics in bacterial infections. *Bull. New York Acad. Med.* 27:199-220, 1951.

However, for every such usage of antimicrobial agents that is justifiable on the basis of experimental data or observed clinical experience there are many uses that have no basis whatever. As a result, the actual prophylactic and ancillary uses of antibiotics account for the great bulk of the present consumption of antibiotics, particularly in this country, and only a very minor fraction of the total amount prescribed is given for specific indications in the treatment of established infections, even after the most generous allowances are made for dosages.

Furthermore, the multiplication of available antibiotics that have overlapping spectrums of activity and the high-pressure advertising and sales methods used by some of their manufacturers have resulted in the use of multiple agents with a minimum of regard to their possible value under such circumstances or to the possible implication of such usages. The toxic effects of antibiotics are well known. In particular, the possibility of sensitizing patients to all these highly important and useful agents need only be mentioned in order that its great importance be realized. Furthermore, the possibility of eliminating from a large number of persons in the population the organisms that are sensitive to all the active antibiotics and of replacement of the flora by organisms that are resistant to them brings up the possibility that very serious consequences may result from the widespread prophylactic use of these important and potentially life-saving agents if we are also to continue to use them for the purpose for which they are primarily intended, namely, the treatment of serious infectious diseases. The increasing frequency of serious and even fatal infections with staphylococci that are resistant to most or even all of the currently available antibiotics is mentioned as an important indication that this danger is not entirely theoretical.

It seems obvious that physicians should acquaint themselves with the proper indications for antibiotic therapy. Whenever possible, they should use dosages of single agents that have proved adequate and effective. The use of multiple agents for simple infections or the use of single agents for prophylactic purposes should be reserved for the types of cases in which there is already adequate proof, on the basis of well authenticated experience, that their use is desirable and may be expected to yield beneficial effects.

HUNTING THE SNARK

One attribute that an editor needs in addition to a knowledge of the ignorance of others, according to Hugh Clegg,* editor of the *British Medical Journal*, is a due sense of his own lack of knowledge. There should be no reasonable excuse, however, for the average moderately perceptive editor's lacking an appreciation of this shortcoming; he is reminded of it often enough, in one way or another.

Dr. Clegg, in a paper devoted primarily to a discussion of the signing of book reviews, mentioned in a previous issue of the *Journal*, had more to say on the general functions of the editor — as well as on his shortcomings.

One of the pitfalls dug in the editor's path is his responsibility for the unsigned editorial, which, "by a generally accepted convention," is supposed to come from his own pen. He thus runs the risk of acquiring an entirely unearned reputation for almost superhuman profundity, which he may actually come to believe in if he is sufficiently tolerant of the ego, — to his eventual and inevitable undoing.

A chief function of the editor, Dr. Clegg points out, is his obligation to say "no" when it would be so much pleasanter to say "yes." It is that responsibility, according to Sir Edward Mellanby, that makes the editor's job important as well, occasionally, as unpleasant.

"An editor has to say 'No,' " Dr. Clegg continues, "to bad taste, bad manners, bad English, bad articles. The corollary, of course, is that he also has to say 'Yes' to a number of things; or else his journal would be like the map in Lewis Carroll's *Hunting of the Snark;* a perfect and absolute blank. It is so much easier to say 'Yes' than to say 'No.' "

The preparation, the correction and the polishing of copy before it is submitted to the printer — its "editing" — is a function that is performed well in first-class editorial offices where experts are usually employed for the purpose, and indifferently or poorly in most others. It is a necessary function, regardless of the heartaches that may result when a cherished masterpiece of phraseology expires on the point of a blue pencil or the choler that may rise when some punctured verbal balloon falls to the ground as its gas escapes.

"Style," Clegg quotes Aristotle as saying, "is the art of being clear without being mean"; he points out that clarity in writing is not necessarily an attribute of the scientific worker, — and that the final responsibility for what appears on the printed page must be the editor's.

Few authors, even professional ones, observe all the rules of good composition. Clear scientific writing is a tricky game, — and often enough, in these hurried days, a man who is writing about a series of acts performed or results obtained is understandably more concerned with the reporting of these things than with the style of the report. Although thoughts may spring full-bodied from the brows of their authors, sentences do not.

Moreover, the usages of a periodical, which have been established for the purpose of concise and lucid presentation, must be observed if its contents are to be uniformly clear and accurate; in scientific writing, whose main purpose is to disseminate information, the language itself should be unobtrusive. The editor, in trying to achieve this objective, must strive to preserve both fluidity and the personal touch that is sometimes the author's most highly prized contribution.

The product of any author needs this final polish, even if he is the professor himself, and the average author can no more give it to his own writing than he can cut his own hair. A journal, when all is said, is not merely a vehicle on which an author hooks a ride or a megaphone by means of which his voice is amplified. It is an organ of expression to which its editorial staff owes a responsibility in the matter of form and content that must take precedence over even the respect that is due to the contributor's sensibilities.

*Clegg, H. On signing reviews. *World Med. Assoc. Bull.* 3:15, 1951.

ECCE FEMINA

The main risk that woman has run in attaining equal suffrage, submitting herself to jury duty and the penalties of traffic violation, entering into business and professional competition with man and assuming in general a position of equality with the usually more muscular sex is that she might thereby jeopardize some part of that superiority over man with which she has been equipped by nature and credited by mutual consent.

Such fears seem to have been unfounded. Instead of descending from the spacious pedestal on which she has borne and reared her children, fed her family and cared for her home, including often enough the annual victory over a furnace and the disposal of its ashes, she has simply stepped over onto another equally elevated platform. She has done more than this; she has frequently, with dignity, poise and even modesty, effected a compromise by straddling the two.

Political suffrage and professional success have added nothing to woman's prestige; they have simply spread it more widely, if a trifle less thickly. The world still has its Ruths and its Naomis, its Aspasias, its Cornelias, its Joans of Arc and its lady editors.

The official entrance of women into the ranks of the physicians is of relatively recent date, although their part in the healing of the sick goes back beyond antiquity — for did not Helen, daughter of Zeus, "presently cast a drug into the wine whereof they drank, a drug to lull all pain and anger, and bring forgetfulness of every sorrow"? Trotula, Rebecca and Constanza, the "ladies of Salerno," were recognized as physicians and practiced the art of medicine in the Middle Ages; the first woman graduate in medicine, Elizabeth Blackwell, received her degree from Geneva College in New York State in 1849 and started a continuous line of female physicians, — some of them eminent, and many of them able and devoted to their difficult duties.

It is an honor to the medical profession of Massachusetts that Dr. Sara M. Jordan, one of those on whom this text is based, a former president of the American Gastro-Enterological Association, was recently chosen to represent medicine at the first Assembly of American Women of Achievement.

SHATTUCK AWARD

THE second Lemuel Shattuck award of the Massachusetts Public Health Association, an award established in 1949, was presented on April 26 to Dr. Henry Dexter Chadwick, of Waltham, who, in his retirement, is continuing a life of singular usefulness as consultant physician of the Channing Home.

Dr. Chadwick has devoted almost his entire career of over a half-century to the service of New England and New England institutions. A former commissioner of public health of the Commonwealth of Massachusetts and one-time president of the Massachusetts Public Health Association, the Massachusetts Tuberculosis League and the National Tuberculosis Association, he is perhaps best known as the organizer of the Ten-Year Program for the Early Detection of Tuberculosis in Children. This important contribution to the universal campaign against tuberculosis has appropriately come to be known as the "Chadwick Clinics."

There is no lack of public-spirited physicians in Massachusetts who might be considered as suitable candidates for this award; it is eminently fitting that Dr. Chadwick should have been chosen as the one among them best qualified to receive it.

A Dr. McConnell, it is said, has applied for a patent for the manufacture of gas from pine wood.
Boston M. & S. J., *June 18, 1851*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

COLBY — Frederick B. Colby, M.D., of Fitchburg, died on May 24. He was in his forty-fourth year.

Dr. Colby received his degree from the University of Lausanne Medical School, Switzerland, in 1937. He was a member of the American Academy of General Practice.

His widow, his mother, two daughters, two sisters and a brother survive.

FULLER — Frederick H. Fuller, M.D., of Walpole, died on March 9. He was in his eightieth year.

Dr. Fuller received his degree from Harvard Medical School in 1894. He was the first school physician of Walpole and also served a number of years on the Board of Health.

His widow, two daughters and a sister survive.

HUNT — George P. Hunt, M.D., of Pittsfield, died on May 22. He was in his seventy-fourth year.

Dr. Hunt received his degree from Harvard Medical School in 1900. He was a member of the American Academy of Pediatrics.

His widow, a son and a daughter survive.

McKechnie — Frederick J. McKechnie, M.D., of Springfield, died on March 6. He was in his seventy-seventh year.

Dr. McKechnie received his degree from Harvard Medical School in 1900. He was a member of the staff of Mercy Hospital and was at one time president of the staff.

A sister survives.

Seaman — James A. Seaman, M.D., of Springfield, died on April 21. He was in his sixty-second year.

Dr. Seaman received his degree from Columbia University College of Physicians and Surgeons, New York City, in 1919. He was secretary of the Springfield Academy of Medicine for twenty-nine years. He was a member of the American Urological Association and the American College of Surgeons and a fellow of the American Medical Association.

His widow, two daughters and a son survive.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Nutrition in Ophthalmology. By John J. Stern, M.D., 8°, cloth, 137 pp. New York: National Vitamin Foundation, Incorporated, 1950. $1.50. (Nutrition Monograph Series, No. 1.)

This monograph constitutes a review of the literature on nutrition and the eye. The text is divided into three main parts: conjunctiva, cornea and sclera; lens and aqueous; and retina, optic nerve and visual act. The various vitamins are discussed in their appropriate places in the text.

Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association: With the comments that have appeared in the Journal of the American Medical Association. 1949. 12°, cloth, 231 pp. Philadelphia: J. B. Lippincott Company, 1950. $2.00.

This annual volume comprises the reports for 1949 and, in addition, reports of lesser importance that were not published in the *Journal of the American Medical Association.*

The Liver: Porta malorum (the gateway to disease). By Kasper Blond, M.D. (Vienna), L.R.C.P., L.R.C.S. (Ed.), L.R.F.P.S. (Glas.); and David Haler, M.B., C.D.P. (Lond.). 8°, cloth, 268 pp., with 36 illustrations. Baltimore: Williams and Wilkins Company, 1950. $5.00.

This monograph discusses the diseases of the liver, and also its role as a detoxicating organ in other diseases. The literature has been thoroughly surveyed, and there is a bibliography of nine pages. The printing was done in Great Britain, and the publishing is excellent.

This small volume should be in all medical libraries, and available to all physicians interested in internal medicine.

The Actinomycetes: Their nature, occurrence, activities, and importance. By Selman A. Waksman, Ph.D., professor of microbiology, Rutgers University, and microbiologist, New Jersey Agricultural Experiment Station. 8°, cloth, 221 pp., with 39 illustrations and 44 tables. Waltham, Massachusetts: Chronica Botanica Company, 1950. New York City: Stechert-Hafner, Incorporated. $5.00. (*Annales Cryptogamici et Phytopathologici.* Vol. IX.)

This comprehensive monograph contains chapters of special interest to physicians and dermatologists relating to the production of enzymes and the growth-producing substances, the antagonistic properties of actinomycetes, the production of antibiotics and the actinomycetes as causative agents of human and animal diseases.

A bibliography of 522 references is appended to the text, and there are indexes of subjects and organisms. The book, which is well published, should be in all collections on the subject.

William Withering of Birmingham, M.D., F.R.S., F.S.L., F.L.S. By T. Whitmore Peck, M.P.S., and K. Douglas Wilkinson, O.B.E., M.D. (Birm.), F.R.C.P. (Lond.). 8°, cloth, 239 pp., with 52 plates. Baltimore: Williams and Wilkins Company, 1950. $4.50.

William Withering is famous for the early use of digitalis in the treatment of diseases of the heart and circulation. He first reported his experiences in *An Account of the Foxglove and Some of Its Medical Uses,* printed in Birmingham in 1785. The authors in this biography have covered the whole period of the life of Dr. Withering, who was interested in botany, chemistry and other subjects, in addition to his medical practice.

The printing was done in Great Britain, and the publishing is excellent. The book should be in all collections on medical history.

Physiology and Anatomy. By Esther M. Greisheimer, M.A., Ph.D., M.D., professor of physiology, Temple University School of Medicine, Philadelphia. Sixth edition. 8°, cloth, 841 pp., with 478 illustrations. Philadelphia: J. B. Lippincott Company, 1950. $4.00.

In this standard textbook for nurses, last published in 1945, the chapters on the physiology of the muscular system and on the blood have been completely revised. The material on the vitamins has been brought up to date. The clearance tests for kidney function have been added, and the chapter on internal secretions has been largely revised. The material is well arranged, and the text well written. There is an excellent index, and the publishing is good.

The 1950 Year Book of Radiology (June, 1949–June, 1950). Radiologic Diagnosis. Edited by Fred J. Hodges, M.D., professor of roentgenology and chairman, Department of Roentgenology, University of Michigan Medical School; and John F. Holt, M.D., associate professor, Department of Roentgenology, University of Michigan Medical School.

Radiation Therapy. Edited by Isadore Lampe, M.D., associate professor, Department of Roentgenology, University of Michigan Medical School; and Robert S. MacIntyre, M.D., assistant professor, Department of Roentgenology, University of Michigan Medical School. 8°, cloth, 480 pp., with 400 illustrations. Chicago: Year Book Publishers, Incorporated, 1950. $6.75.

This yearbook is well arranged and gives a valuable summary of the current literature in the field of radiology. The references are carried as footnotes on the pages, and there are indexes of subjects and authors. The publishing is excellent, and the volume should be in all medical libraries and in the libraries of radiologists and other interested persons.

Health Instruction Yearbook 1950. Compiled by Oliver E. Byrd, Ed.D., M.D., F.A.P.H.A., professor of health education and director, Department of Hygiene, School of Education, Stanford University. With a foreword by Jesse F. Williams, M.D., Sc.D. 8°, cloth, 270 pp. Stanford, California: Stanford University Press, 1950.

This eighth volume of the yearbook follows the pattern of previous years. It covers the period from July, 1949, to June, 1950. Condensations of 255 articles selected by the editor from 1628 publications are published in the book. The text is divided into twenty-one categories. A bibliography of the articles selected is appended to the text. There are indexes of authors and subjects, and the book is well published. It should be in all collections on public health.

Emergencies in Medical Practice. Edited by C. Allan Birch, M.D., F.R.C.P., physician, Chase Farm Hospital, Enfield. Second edition. 8°, cloth, 564 pp., with 131 illustrations. Baltimore: Williams and Wilkins Company, 1950. $5.50.

In this second edition of a composite book, first published in 1948, the text has been revised and chapters on skin diseases, eye diseases, anesthesia and the postoperative state have been added. Twenty-two specialists have contributed to the book. There is a good index, and the publishing is good. The printing was done in Great Britain.

Medical Jurisprudence and Toxicology. By John Glaister, J. P., D.Sc., M.D., F.R.S.E., of the Inner Temple, barrister-at-law, Regius Professor of Forensic Medicine, University of Glasgow. Ninth edition. 8°, cloth, 755 pp., with 284 illustrations. Baltimore: Williams and Wilkins Company, 1950. $7.00.

This standard work, first published in 1902, has been revised and brought up to date. The necessary changes have been made to bring the text into conformity with British law. There is a comprehensive index, and the publishing is excellent. The printing was done in Great Britain. The book should be in all collections on medicolegal medicine and toxicology.

Renal Diseases. By E. T. Bell, M.D., professor of pathology, University of Minnesota Medical School. Second edition. 8°, cloth, 448 pp., with 123 illustrations and 4 color plates. Philadelphia: Lea and Febiger, 1950. $8.00.

Dr. Bell has had at his disposal about 18,000 additional autopsies, and accordingly a larger group of cases has been available for study since the publication of the first edition. The chapters on tubular diseases and extrarenal azotemia have been enlarged. The recent literature has been incorporated in the text. There is a good index. The book is well published and should be in all collections on the subject.

Cancer of the Colon and Rectum: Its diagnosis and treatment. By Fred W. Rankin, M.A., M.D., LL.D., Sc.D., surgeon, St. Joseph's and Good Samaritan hospitals, Lexington, Kentucky, and clinical professor of surgery, University of Louisville School of Medicine; and A. Stephens Graham, M.D., M.S. (in surgery), surgeon, Stuart Circle Hospital, Richmond, Virginia, and associate professor of surgery, Medical College of Virginia. Second edition. 8°, cloth, 427 pp., with 148 illustrations. Springfield, Illinois: Charles C Thomas, 1950. $7.50.

In this new edition of a special book, first published in 1939, the text has been revised and brought up to date. It presents a survey of the current knowledge on the subject. There are indexes of authors and subjects. The book should be in all collections on cancer and the gastrointestinal tract.

Colloid Chemistry: Theoretical and applied. By selected international contributors. Collected and edited by Jerome Alexander. Volume VII. *Theory and Methods: Biology and medicine; technological applications.* New York: Reinhold Publishing Corporation, 1950. $15.00.

This particular volume of a large set is of special interest to physicians and biologists. It contains 193 pages on biology and on various aspects of colloid chemistry and medicine. It is sold separately. There are indexes of authors and subjects, and the publishing is excellent.

An Integrated Practice of Medicine. Volume V. By Harold T. Hyman, M.D. 8°, cloth, 734 pp. Philadelphia: W. B. Saunders Company, 1950. $10.00. (*Progress Volume: Modern developments in therapeutics and methods of treatment.*)

This progress volume supplements the four volumes of the treatise by Dr. Hyman previously published and surveys the pertinent current literature on internal medicine. The material is arranged in alphabetical order. The volume is concluded with a series of important indexes, signs and symptoms to Volumes I–V, general subject index to Volumes I–IV and index of illustrations to Volumes I–V, and a separate index for Volume V on progress. This volume should be acquired by libraries and physicians possessing the set.

Advances in Internal Medicine. Volume IV. Editors: William Dock, M.D., Long Island College of Medicine, Brooklyn, New York; and I. Snapper, M.D., Mount Sinai Hospital, New York City. 8°, cloth, 549 pp., with illustrations. Chicago: Year Book Publishers, Incorporated, 1950. $10.00.

This new volume contains nine articles on special subjects of interest to the internist. They include a discussion of nitrogen mustards in the treatment of neoplastic disease, the use of radioactive isotopes in medicine, brucellosis, neuromuscular disorders, the use of sodium depletion in therapy, clinical use of anticoagulants, hepatitis, cirrhosis of the liver and hepatic tests, and the vascular physiology of hypertension. Lists of references are appended to the various articles, and there are indexes of authors and subjects, and a cumulative author and subject index to volumes I-IV. The book is recommended for all medical libraries.

The Psychoanalytic Study of the Child. Volume V. 8°, cloth, 410 pp. New York: International Universities Press, Incorporated, 1950. $7.50.

This volume, in addition to various papers on psychoanalysis, contains the papers read at a symposium on psychoanalysis and developmental psychology at the meeting of the American Psychoanalytic Association, Detroit, April 29, 1950. The complete series of this publication should be in all collections on the subject.

Progress in Gynecology. Volume II. Edited by Joe V. Meigs, M.D., clinical professor of gynecology, Harvard Medical School; chief of staff of the Vincent Memorial Hospital, the Gynecological Service of the Massachusetts General Hospital, surgeon, Pondville Hospital, and gynecologist, Palmer Memorial Hospital; and Somers H. Sturgis, M.D., clinical associate in gynecology, Harvard Medical School, and assistant surgeon, Massachusetts General Hospital. 8°, cloth, 821 pp., with illustrations. New York: Grune and Stratton, 1950. $9.50.

This composite volume is the joint work of 78 contributors. For the first time British and other European specialists have contributed to the book. New material has been included, and the text has been revised and in many cases rewritten. There is a good index, and the publishing is excellent. The book should be in all medical libraries and in all collections on gynecology.

NOTICES

ANNOUNCEMENT

Dr. Robert S. Thomson announces the removal of his office to 56 Elm Street, Fitchburg.

NAVAL RESERVE VOLUNTEER MEDICAL UNIT NO. 1-1

A meeting of the Naval Reserve Volunteer Medical Unit No. 1-1 will be held at the Children's Hospital, 300 Longwood Avenue, Boston, on June 27, at 7:30 p.m. Rear-Admiral Sterling S. Cook, MC, USN, district medical officer, First Naval District, will speak on the subject "The Teaching Program in Our Naval Hospitals."

Physicians and medical students are cordially invited to attend.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

CONFERENCE PROGRAM

9–10 a.m.

Tuesday, June 19 — Dermatologic Manifestations of Disease. Dr. James F. Patterson.

Wednesday, June 20 — Factors that Influence the Level of Circulating Eosinophils in the Blood. Dr. Charles D. Bonner.

Friday, June 22 — Anemia of Leukemia and Lymphoma. Dr. Charles L. Crockett, Jr.

Tuesday, June 26 — Simmonds's Disease. Dr. Henry H. D. Sterrett, Jr.

Wednesday, June 27 — Gastroenterology Clinic. Dr. Malcolm M. Stanley.

Friday, June 29 — Cardiac Metabolism Studied Both in vitro and in vivo. Dr. Robert E. Olson.

Conferences are held in the Pratt Lecture Hall.
All exercises are open to the medical profession.

(*Notices concluded on page xv*)